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medical devices

Regulatory Requirements for Medical Devices

A Workshop Manual

Fourth Edition

CENTER FOR
DEVICES AND
RADIOLOGICAL HEALTH
DRH

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
Public Health Service
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(Continued on inside back cover)

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Regulatory Requirements for Medical Devices

A Workshop Manual

Prepared by the
Division of Small Manufacturers Assistance
Office of Training and Assistance

Project Officers
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May 1989

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U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
Public Health Service
Food and Drug Administration
Center for Devices and Radiological Health
Rockville, Maryland 20857

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Washington, D.C. 20402

FOREWORD

In October 1982, the Food and Drug Administration established the Center for Devices and Radiological Health (CDRH) by merging the Bureau of Medical Devices and the Bureau of Radiological Health.

The Center develops and implements national programs to protect the public health in the fields of medical devices and radiological health. These programs are intended to assure the safety, effectiveness and proper labeling of medical devices, to control unnecessary human exposure to potentially hazardous ionizing and nonionizing radiation, and to ensure the safe, efficacious use of such radiation.

The Center publishes the results of its work in scientific journals and in its own technical reports. These reports provide a mechanism for disseminating results of CDRH and contractor projects. They are sold by the Government Printing Office and/or the National Technical Information Service.

We welcome your comments and requests for further information.

John C. Villforth

John C. Villforth
Director
Center for Devices and
Radiological Health

PREFACE

The Medical Device Amendments of 1976 mandated the establishment of "...an identifiable office to provide technical and other non-financial assistance to small manufacturers of medical devices to assist them in complying with the requirements of the Federal Food, Drug, and Cosmetic Act." The Division of Small Manufacturers Assistance (DSMA) in the Office of Training and Assistance was established to meet these requirements. DSMA sponsors workshops and conferences to provide small device firms with firsthand working knowledge of device requirements and compliance policies.

The materials in this manual cover the range of basic regulatory requirements that all manufacturers must consider when they begin marketing a medical device. It is important to know these requirements, how to determine which ones are pertinent to your particular situation, and the proper sequence or timetable for fulfilling them. Although prepared specifically for use in DSMA's Regulatory Requirements Workshops, this publication will prove useful as a reference on establishment registration, device listing, labeling requirements, classification, premarket notification [510(k)], premarket approval (PMA) and other topics of significance to device manufacturers.

The DSMA staff and many other persons in CDRH provided invaluable assistance in preparing these materials, formulating regulatory interpretations, and presenting the workshops.

For further information, contact the appropriate office within CDRH or call DSMA toll free at 800-638-2041. Comments on this workbook, and other DSMA activities, are always welcome.

Joseph S Arcarese

Joseph S. Arcarese
Director
Office of Training and Assistance

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ABSTRACT

R. Parr, A. Barcome. Regulatory Requirements for Medical Devices: A Workshop Manual. HHS Publication FDA 89-4165 (May 1989) (pp. 364).

This manual covers the range of basic regulatory requirements that all manufacturers must consider when they begin marketing a medical device. The materials it contains are useful for guidance and reference on establishment registration, device listing, and labeling requirements, classification, premarket notification [510(k)], premarket approval (PMA) and other topics of significance to device manufacturers.

OVERVIEW OF THE MEDICAL DEVICE AMENDMENTS

With the passage of the Federal Food, Drug, and Cosmetic Act (the Act) of 1938 the Food and Drug Administration (FDA) was authorized for the first time to regulate medical devices in order to assure their safety. This legislation defined a medical device as "any instrument, apparatus, or contrivance, including any of its components or parts, intended for use in the diagnosis, cure, treatment, or prevention of disease in man or other animals."

The Act provided for regulation of adulterated or misbranded medical devices that were entered into interstate commerce. Devices were considered adulterated if they included any filthy, putrid, or decomposed substance, or if they were prepared, packed, or held under unsanitary conditions. They were considered to be misbranded if their labeling was false or misleading or if it failed to identify manufacturer, packer or distributor or to disclose the quantity of its contents.

When a device was determined to be in violation of the Act, FDA's new authority empowered it to seize the product; request an injunction against its production, distribution, or use; and/or recommend criminal prosecution of the manufacturer or other persons responsible for its manufacture or distribution.

The 1938 Act, however, was limited in its effectiveness because it did not require, as it did for drugs, any form of premarket approval for devices entered into interstate commerce. As a result, any device could be marketed without having undergone federally approved testing procedures. Most of FDA's actions and litigations during this period concentrated on assuring proper labeling and on removing quack or fraudulent devices from the marketplace.

Following World War II, much of the military technology that had been developed was redirected toward medicine. Medical technology rapidly improved; devices became more complicated and more critical to patient care. Technological advances in electronics, plastics, metallurgy, ceramics, and engineering design affected all aspects of medicine and led to development of such devices as cardiac pacemakers and renal catheters, surgical implants, artificial vessels and heart valves, intensive care monitoring units, intrauterine devices, replacement joints, and other diagnostic and therapeutic products. With the growth of clinical laboratories, the ability to diagnose increased enormously.

By the early sixties, it became clear that the provisions of the 1938 Act were not adequate to regulate these new, more complex devices. Because of the lack of sufficient regulation, for example, anyone with an understanding of electronics and the concepts involved could design, produce, and market a cardiac pacemaker without any standardized testing. The pacemaker might then be implanted before any problems associated with its use were encountered. Problems with critical devices such as these underscored the need for new device legislation.

Before passage of the Medical Device Amendments in May 1976, the courts filled this regulatory gap by ruling that some medical devices were, in fact, drugs and could be regulated as such. Examples of products that were regulated as drugs included intrauterine devices (IUDs), contact lenses, weight-reducing kits, and some in vitro diagnostic products.

In 1969, a study group headed by Dr. Theodore Cooper was formed to examine problems associated with medical devices and to develop concepts for new legislation. This group, known as the "Cooper Committee," reported that over a 10-year period, problems associated with medical devices had resulted in 10,000 injuries, 751 of them resulting in death.

The Committee recommended that future device legislation establish a three-tiered system for regulating devices:

- a class for devices that would be exempt from any premarket clearance and any performance standards;
- another class for devices that could be marketed without premarket clearance (provided adequate safety and effectiveness standards or data were available, with which they would have to comply); and
- a third class of devices, intended particularly for critical or life-supporting devices, that in all cases would be required to undergo a premarket clearance process because adequate performance standards to assure their safety or effectiveness did not exist.

On May 28, 1976, President Gerald R. Ford signed into law the Medical Device Amendments to the Act. The purpose of the Amendments is to ensure that medical devices are safe and effective, and properly labeled for their intended use. In order to accomplish this mandate, the Amendments provide FDA with authority to regulate devices during most phases of their development, testing, production, distribution, and use.

For the first time, the 1976 Amendments clearly distinguished between devices and drugs. They define a medical device as: "any instrument, apparatus, implement, machine, contrivance, implant, in vitro reagent, or other similar or related article, including any component, part, or accessory, which is:

- recognized in the official National Formulary, or the United States Pharmacopeia, or any supplement to them;
- intended for use in the diagnosis of disease or other conditions, or in the cure, mitigation, treatment, or prevention of disease, in man or other animals; or
- intended to affect the structure or any function of the body of man or other animals; and
- does not achieve any of its principal intended purposes through chemical action within or on the body of man or other animals and which is not dependent upon being metabolized for the achievement of any of its principal intended purposes."

A major distinction between drugs and devices is made in the final portion of the definition. Those products that are not metabolized or are not dependent upon being metabolized in order to achieve their major intended purpose are to be regulated as devices and not drugs.

The definition of a "device" also includes in vitro diagnostic products that aid in the diagnosis of disease by using human or animal components to cause chemical reactions, fermentation, and the like. In these instances the device is not placed in or permanently attached to the body

Finally, a medical device also includes any article intended for use in the diagnosis of conditions other than disease. An example of this would be a device used to diagnose pregnancy.

Approximately 1700 types of medical devices are regulated under the legislation. The range of devices is diverse, including bandages, thermometers, ECG electrodes, IUDs, cardiac pacemakers, and hemodialysis machines. In addition, these devices fall into five nonmutually exclusive categories defined on the basis of procedures and utilization:

- Over-the-Counter Devices - devices that can be purchased by the consumer without a prescription;
- Prescription Devices - devices for which adequate directions for use cannot be devised in order to permit lay persons to use the device safely and effectively unless under the supervision and direction of a practitioner;
- Investigational Devices - devices still in developmental stages and used on human subjects only for purposes of developing safety and effectiveness data;
- Custom Devices - devices ordered from a manufacturer by health professionals to conform to their special needs or those of an individual patient and not generally available to or generally used by other practitioners; and
- Critical Devices - devices as defined in the Good Manufacturing Practice (GMP) regulation that are life-sustaining, life-supporting or intended to be implanted into the human body and whose failure can be reasonably expected to result in a significant injury.

The term "medical device" describes a large and diverse set of products. Regulation of these products is a difficult and complicated process, not only because of sheer volume and variety, but also because of their increasing importance in the delivery of patient health care.

The information in this manual should, if applied, simplify the steps in marketing medical devices. Except the GMP regulation which is discussed in a separate DSMA manual, this manual covers the basic regulatory requirements that apply to medical devices including registration and listing, premarket notification, premarket approval, investigational device exemptions, labeling, and classification.

CONTACT POINTS

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Deputy Director, CDRH	443-4690	HFZ-1
Director, Office of Training and Assistance	443-2845	HFZ-200
Division of Small Manufacturers Assistance	443-6597 (or 800-638-2041)	HFZ-220
Office of Health Affairs	427-7034	HFZ-70
Director, Office of Compliance	427-7167	HFZ-300
Division of Compliance Programs	427-7215	HFZ-331
Good Manufacturing Practices Branch	427-7194	HFZ-332
Division of Compliance Operations	427-7218	HFZ-320
Device Regulatory Guidance Branch (Labeling)	427-8040	HFZ-323
Division of Product Surveillance	427-8156	HFZ-340
Registration and Product Listing Branch	427-7190	HFZ-342
Director, Office of Device Evaluation	427-7004	HFZ-400
Division of Anesthesiology & Neurology Devices	427-7226	HFZ-430
Division of OB/GYN, Ear, Nose, Throat & Dental Devices	427-7555	HFZ-470
Division of Cardiovascular Devices	427-7559	HFZ-450
Division of Gastro/Urology & General Use Devices	427-7750	HFZ-420
Division of Clinical Laboratory Devices	427-7550	HFZ-440
Division of Ophthalmic Devices	427-7940	HFZ-460
Division of Surgical & Rehabilitation Devices	427-7238	HFZ-410
Radiological Devices	427-7514	HFZ-430
Program Operations Staff:		
IDE	427-8162	HFZ-403
PMA	427-7445	HFZ-402
510(k)	427-8162	HFZ-401
Reclassification	443-8162	HFZ-403

DEVICE ADVISORY COMMITTEES AND PANELS

Anesthesiology and Respiratory Therapy Devices Panel	427-7226	HFZ-430
Circulatory System Devices Panel	427-7594	HFZ-450
Clinical Chemistry and Clinical Toxicology Devices Panel	427-7550	HFZ-440

Dental Devices Panel	427-7555	HFZ-470
Ear, Nose and Throat Devices Panel	427-7555	HFZ-470
Gastroenterology-Urology Devices Panel	427-7750	HFZ-420
General and Plastic Surgery Devices Panel	427-7238	HFZ-410
General Hospital and Personal Use Devices Panel	427-7750	HFZ-420
Hematology and Pathology Devices Panel	427-7550	HFZ-440
Immunology Devices Panel	427-7550	HFZ-440
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Ophthalmic Devices Panel	427-7940	HFZ-460
Orthopedic and Rehabilitation Devices Panel	427-7238	HFZ-410
Radiologic Devices Panel	427-7514	HFZ-430

1 GENERAL CONTROLS

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INTRODUCTION

The 1976 Medical Device Amendments (often referred to as the Amendments) supplement the provisions of the Federal Food, Drug, and Cosmetic Act (referred to as the Act) by providing the Food and Drug Administration (FDA) with significant additional authority to assure safety and effectiveness in devices intended for human use.

Three regulatory classes were established for this purpose, based on the degree of control necessary for assuring the safety and effectiveness of various types of devices:

- o Class I - General Controls
- o Class II - Performance Standards
- o Class III - Premarket Approval

GENERAL CONTROLS

General controls consist of the basic requirements of the Amendments that apply to all medical devices, including those in Class II and Class III, unless specifically exempted. Class I devices, however, are subject only to general controls. Class II and III devices are subject to additional requirements.

General controls include the provisions of the Act pertaining to:

- o adulteration;
- o misbranding;
- o banned devices;
- o notification; and repair, replacement or refund;
- o records and reports; and
- o restricted devices.

General controls also require device manufacturers or other designated persons, unless specifically exempted, to perform the following activities:

- o establishment registration and device listing;
- o premarket notification [510(k)]; and
- o good manufacturing practices (GMPs).

Adulteration

Medical devices, which are subject to adulteration provisions of the Act under Section 501, are considered to be adulterated if they:

- include any filthy, putrid, or decomposed substance or are prepared, packed or held under insanitary conditions;
- are in a container composed, in whole or part, of any poisonous or deleterious substance;
- contain, for the purpose of coloring only, an unsafe color additive;
- differ in strength from, or their purity or quality falls below, that which they claim to represent;
- do not comply with an applicable performance standard;
- fail to comply with the requirements for an approved premarket approval application or product development protocol;
- are banned devices;
- violate the Good Manufacturing Practices (GMP) regulation; or
- fail to comply with the Investigational Device Exemption regulation.

Misbranding

The misbranding provisions of the Act are contained in Section 502. They cover various aspects of labeling requirements for drugs and devices.

(For an introductory outline on these requirements, see the chapter on "Labeling.")

Banned Devices

Under Section 516, FDA is authorized to ban a device that presents a substantial deception or unreasonable and substantial risk of illness or injury.

If the FDA determines, after considering all available data and consulting with the appropriate advisory panel, that the deception or risk involved cannot be corrected by a change in labeling, a proceeding to ban a device is initiated upon publication of a proposed regulation in the FEDERAL REGISTER. An opportunity for hearing and final action on the regulation follows the proposal. The ban can take effect immediately if the deception or risk presents an immediate, direct danger to public health.

Notification; and Repair, Replacement or Refund

The notification; and repair, replacement or refund portions of the Act (Section 518) were designed to protect the public from faulty and fraudulent devices by assuring that hazardous products in the hands of consumers and other users will be repaired, replaced, or their purchase price refunded.

Under Section 518(a) of the Act. FDA may require manufacturers or other individuals to notify all health professionals who prescribe or use a device and any other persons (including manufacturers. importers. distributors. retailers. and device users) of the health risks resulting from the use of the violative device.

Section 518(b) of the Act authorizes FDA. after offering an opportunity for an informal hearing. to order manufacturers. importers. or distributors to repair. replace. or refund the prices of devices that present unreasonable health risks. Where practical. FDA will use regulatory approaches other than Section 518.

Records and Reports

FDA may promulgate under Section 519 regulations that require manufacturers. importers. and distributors of devices to maintain sufficient records and reports to assure that devices are not adulterated or misbranded. The Medical Device Reporting (MDR) regulation which is discussed in this chapter is an example of such a rule.

Regulations promulgated under Section 519 of the Act may not impose requirements that are unduly burdensome. They must state the reason and purpose for requiring procedures and submission of reports or information. They may not require disclosure of patient identity; and manufacturers. importers. or distributors cannot be required to maintain or submit reports or information not in their possession.

Records and report requirements do not apply to licensed practitioners using devices solely in the course of their practice. or manufacturers and importers who use devices solely for teaching or research. or other persons exempt by regulation.

Restricted Devices

Under Section 520(e). FDA is authorized to restrict the sale. distribution or use of a device if it is determined that there cannot otherwise be reasonable assurance of its safety and effectiveness.

Restricted status is determined on the basis of a device's intended use and on whether it can be adequately labeled for use by nonprofessionals. Restrictions must be stated on the label of the restricted device. and restricted devices can only be sold either on written authorization by a licensed practitioner or under conditions specified by regulation.

Registration and Listing

Section 510 of the Act requires that device manufacturers annually register their establishments and list their devices in commercial distribution. (For an introductory outline on these requirements. see the chapters on "Establishment Registration" and "Medical Device Listing.")

Premarket Notification

Under Section 510(k) of the Act. a manufacturer must notify the FDA at least 90 days before introduction into interstate commerce for commercial distribution. "post-enactment" devices. i.e.. devices introduced into the marketplace after the Amendments were enacted on May 28. 1976. (This requirement is not applicable to Class III transitional devices or to exempt Class I devices.)

The 510(k) requirement applies regardless of classification or the nature of the device, and whenever an existing device is modified in a way that may significantly affect its safety and effectiveness. (For an introductory outline, see the chapter on "Premarket Notification [510(k)].")

Good Manufacturing Practices

Under Section 520(f), the GMP regulation is authorized for the control of the methods used in, and the facilities and controls used for, the manufacturing, packing, storage, and installation of devices.

The GMP regulation contains general quality assurance (QA) requirements in areas of concern to all manufacturers of finished devices. It covers the following general areas:

- organization and personnel;
- buildings;
- controls for components, processes, packaging and labeling;
- device holding, distribution and installation;
- device evaluation;
- device and manufacturing records;
- complaints; and
- QA system audits.

Examples of records and reports required by the GMP regulation are:

- a device master record prepared, dated and signed by a designated individual(s) which includes or references all specifications, production processes, procedures and environmental requirements; and quality assurance checks and apparatus, as well as appropriate packaging methods and specifications (plus additional requirements for critical devices);

- a device history record indicating that devices are manufactured in accordance with the device master record and, if applicable, containing control numbers, along with the dates and quantitites of manufacture and distribution (plus additional requirements for critical devices); and

- complaint files (on device identity, quality, durability/reliability, safety, effectiveness and performance) required to be maintained and reviewed by a formally designated unit and/or individual(s).

Additional Requirements

In addition to meeting the minimum requirements under general controls, Class II and Class III devices are also subject to additional requirements.

Devices for which general controls alone are insufficient to assure safety and effectiveness, but for which enough information is known to allow for development of performance standards that would provide such assurance, are Class II devices. These devices must comply with, on dates prescribed by FDA, applicable standards developed under Section 514. Until such standards are established by regulation, only general controls will apply to such devices. Class II accounts for approximately 50 percent of all devices, including such products as hearing aids, catheters, and hard contact lenses.

Class III, the most stringent category, is reserved for devices that are life-supporting or life-sustaining, or of substantial importance in preventing impairment of human health. Malfunction of such devices would pose a potential unreasonable risk of illness or injury to the patient. Manufacturers of devices assigned to Class III must, therefore, obtain premarket approvals from FDA before their devices may be introduced into interstate commerce for purpose of commercial distribution. Approximately 10 percent of all devices have been assigned to Class III, including cardiac pacemakers, intraocular lenses, and heart valve replacements. (For a more detailed treatment of Class III requirements, see the chapter on "Premarket Approval.")

Medical Device Reporting

Since December 13, 1984, manufacturers and initial distributors of medical devices have been required to comply with the Medical Device Reporting (MDR) regulation, 21 CFR Part 803, if they are required to register under Part 607 or 807 with the FDA. FDA is requiring manufacturers and initial distributors of devices (referred to as "importers" in the MDR rule) to report to FDA whenever the firms become aware of information that reasonably suggests that one of its marketed devices (those in commercial distribution): (1) may have caused or contributed to a death or serious injury, or (2) has malfunctioned and that the device or any other device marketed by the firm would be likely to cause or contribute to a death or serious injury if the malfunction were to reoccur.

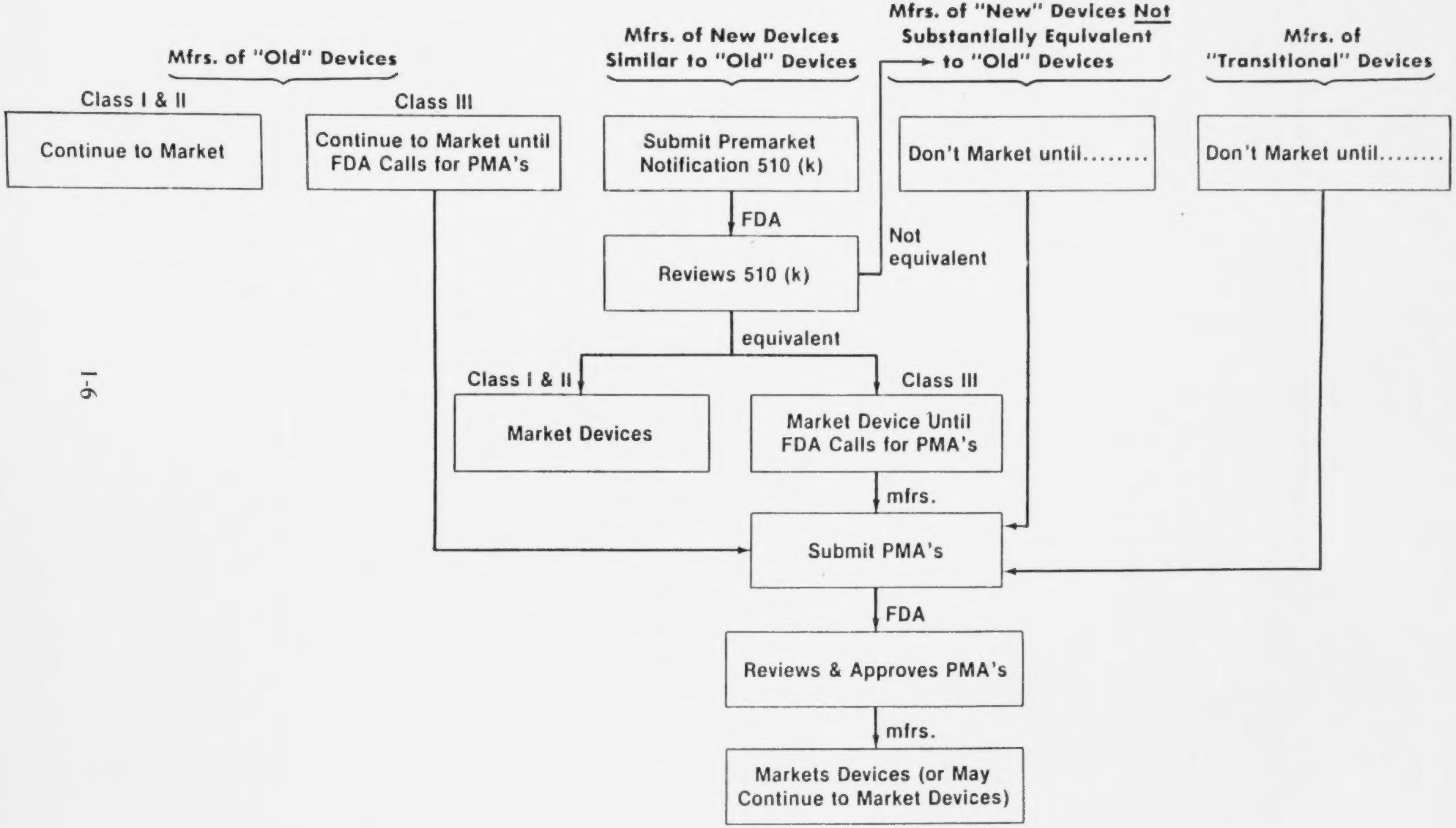
Reports of death or serious injury must be telephoned to FDA at (301) 427-7500 no later than 5 calendar days from the time the importer or manufacturer receives the information. Additionally, telephone reports must be followed up by written reports to FDA within 15 working days from the time the importer or manufacturer receives the information for all reports of death and serious injury and all reports of malfunctions likely to cause or contribute to a death or serious injury.

Importers and manufacturers of devices are required to establish and maintain an MDR file and to permit any authorized FDA employee at all reasonable times to have access to and to copy and verify the records contained in this file. FDA considers any expression of dissatisfaction, be it oral or written, regarding the identity, quality, durability, reliability, safety, effectiveness, or performance of a device, to be a complaint. However, not all complaints meet the MDR reporting criteria.

If you need a copy of the MDR regulation or have general questions about the requirements, you should call the Division of Small Manufacturers Assistance toll free at 800-638-2041. If you have specific questions about whether or not an actual situation must be reported, you should call (301) 427-8100. Written reports and inquiries should be addressed to:

Center for Devices and Radiological Health
Division of Product Surveillance
Device Monitoring Branch, HFZ-343
5600 Fishers Lane
Rockville, Maryland 20857

Bringing Devices to Market


Mfrs. of "Old" Devices
Class I & II
Continue to Market
Class III
Continue to Market until FDA Calls for PMA's
Mfrs. of New Devices Similar to "Old" Devices
Submit Premarket Notification 510 (k)
FDA
Reviews 510 (k)
Not equivalent
equivalent
Class I & II
Market Devices
Class III
Market Device Until FDA Calls for PMA's
mfrs.
Mfrs. of "New" Devices Not Substantially Equivalent to "Old" Devices
Don't Market until........
Mfrs. of "Transitional" Devices
Don't Market until........
Submit PMA's
FDA
Reviews & Approves PMA's
mfrs.
Markets Devices (or May Continue to Market Devices)

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INTRODUCTION

Classification is the cornerstone of device regulations. In this process, the Food and Drug Administration (FDA) places all medical devices into one of three classes. The class dictates the degree or extent of regulatory control needed to assure safety and effectiveness of the device. FDA is required to classify all devices intended for human use under Section 513 of the Federal Food, Drug, and Cosmetic Act (the Act).

The two purposes of classification are:

- o to evaluate devices intended for human use and determine into which of the three following classes they fall; and
- o to provide manufacturers and importers of devices with a means of identifying the regulatory controls that apply to the devices they manufacture or import.

CLASS I - GENERAL CONTROLS

Class I, the least stringent regulatory category, consists of devices for which general controls are sufficient to assure safety and effectiveness. However, these basic regulatory controls also apply to Class II and Class III devices. General controls are explained in Chapter 1.

Examples of Class I devices include enema kits, elastic bandages, and pipetting and diluting systems for clinical use.

Certain Class I devices are exempted from one or two general controls: the premarket notification and the good manufacturing practices requirements.

These exemptions apply under certain conditions and situations. To check out possible exemptions, refer to the list in the chapter on Premarket Notification.

Certain exemptions for devices are still in the proposal stage, even though the device itself has been finally classified.

CLASS II - PERFORMANCE STANDARDS

Class II consists of those devices for which general controls are insufficient to assure safety and effectiveness, and existing information is sufficient to establish a performance standard that provides such assurance.

In addition to complying with general controls, Class II devices are required to meet, on a date prescribed by FDA, an applicable standard developed under Section 514. Until standards are established by regulation, general controls will continue as the sole controls for such devices. Examples of Class II devices are powered wheelchairs and some pregnancy test kits.

CLASS III - PREMARKET APPROVAL

Class III consists of devices for which insufficient information exists to assure that general controls and performance standards provide reasonable assurance of safety and effectiveness.

Generally, devices fall into Class III if they:

- o are represented to be life sustaining or life-supporting;
- o are implanted in the body; or
- o present potential unreasonable risk of illness or injury.

Manufacturers of preamendment Class III devices (i.e., devices marketed before May 28, 1976) and of postamendment devices (those marketed after that date) which are substantially equivalent to a Class III device have 30 months after the final classification of the device into Class III before FDA can require submission of a premarket approval application (PMA).

Devices proposed for marketing after May 28, 1976, that are not substantially equivalent to a preamendment device are automatically classified into Class III, and cannot be marketed without an approved application for premarket approval from FDA.

Examples of preamendment Class III devices are implantable pacemaker pulse generators, automated heparin analyzers, and infant radiant warmers.

THE CLASSIFICATION PROCESS

Groups of experts have been established, originally designated as panels, who for over a decade have been providing advice and recommendations to FDA on device classification. After receiving these recommendations, FDA determines which class is appropriate.

As of June, 1988, there are 16 operating classification advisory committees:

- o Circulatory Systems Devices
- o Clinical Chemistry and Clinical Toxicology Devices
- o Hematology and Pathology Devices
- o General Hospital and Personal Use Devices

- Gastroenterology-Urology Devices
- Immunology Devices
- Microbiology Devices
- Obstetrics-Gynecology Devices
- Radiology Devices
- Ophthalmic Devices
- Ear. Nose. and Throat Devices
- Dental Devices
- Anesthesiology and Respiratory Therapy Devices
- Neurology Devices
- Orthopedic and Rehabilitation Devices
- General and Plastic Surgery Devices

Each panel is composed of eight members. six voting and two nonvoting. Voting members are appointed from the research and medical communities. One nonvoting member represents industry and the other represents consumer interests.

The panel review process has taken the following factors into consideration when determining whether there is reasonable assurance that the device is safe and effective for its intended use:

- persons for whose use the device is intended;

- conditions of use for the device;

- probable benefit to health from use of the device weighed against any probable injury or illness from such use: and

- reliability of the device.

To facilitate panel review of devices. FDA developed a classification scheme. which consisted of two questionnaires. one for general devices and the other for in vitro diagnostic devices. designed to determine and identify characteristics of individual devices. Questions used were intended to elicit information on each device. and to determine the appropriate class of the device.

In addition to the classification scheme. panel members also completed a supplemental data sheet for each device they reviewed.

Once a panel completed its review of a device. it submitted. along with its classification recommendation:

- a summary of reasons for the recommendation;
- a summary of data upon which its recommendation was based;
- an identification of any unreasonable risks to health presented by the device;
- exemption recommendations for Class I devices; and
- priority recommendations for Class II and Class III devices.

FDA reviewed a panel's recommended classification for each device and decided whether to accept it. If the FDA assigned the device to a different class than that recommended by the panel. it documented its reasons.

Both the panel recommendation and the proposed FDA classification were published in the FEDERAL REGISTER as a proposed classification regulation. All interested parties were allowed 60 days in which to comment. After these comments were received and evaluated, a final notice classifying the device was published in the FEDERAL REGISTER. This final regulation became effective, and the device legally classified, usually 30 days after publication of the FEDERAL REGISTER notice. The FDA has published 16 final classification regulations classifying approximately 1700 different generic types of medical devices.

TRANSITIONAL DEVICES

In accordance with the expanded definition of the term "device" established by the Amendments, certain products previously regulated as new drugs or antibiotics are now regulated as devices. Under the transitional provisions of Section 520(l) of the Act, these devices previously regulated as new drugs or antibiotics are automatically placed in Class III requiring premarket approval before commercial distribution. Devices subject to approved new drug applications (NDAs) are regarded as Class III devices with approved PMAs.

On December 16, 1977, FDA published a notice in the FEDERAL REGISTER containing two lists of devices previously regulated as new drugs or antibiotics. One list contains those devices for which premarket approval is needed; the other list, those for which premarket approval is not needed. On September 5, 1980, a FEDERAL REGISTER notice identified four biological in vitro diagnostic products previously regulated as new drugs for which a PMA is required before commercial distribution.

CLASSIFICATION INFORMATION

As provided in Section 513(g) of the Act, manufacturers may contact FDA to obtain current information on the classification status of a device.

The written 513(g) request should be sent to the Food and Drug Administration, Document Mail Center (HFZ-401), 5600 Fishers Lane, Rockville, Maryland 20857.

CHANGES IN DEVICE CLASSIFICATION

The Act contains provisions for changing the classification of a device. Changes in classification are based on FDA's receipt of new information about a device.

FDA may, on its own initiative or in response to a petition by an interested party (including manufacturers), change a device's classification by regulation. The FDA may also revoke any regulation or requirement under Section 514 (Performance Standards) or 515 (Premarket Approval) that pertains to the device. The sections of the Act that apply to changing classification are 513(e), 513(f), 514(b), 515(b)(2) and 520(l)(1).

A manufacturer who wishes to have a device reclassified to a lower class must convince the FDA that the less stringent class requirements will be sufficient to provide reasonable assurance of safety and effectiveness. If the manufacturer's petition requests that the device be moved from Class III to Class II, the petition must also include information to demonstrate that sufficient information exists for developing a performance standard to reasonably assure FDA that the device is safe and effective for its intended use(s).

Once FDA has determined that a classification petition contains no deficiencies that would preclude reaching a decision on it, the petition is referred to an appropriate classification advisory committee for review and recommendation to approve or deny. The committee's recommendation is then published in the FEDERAL REGISTER for comment.

After FDA has completed its review of the comments, it notifies the petitioner by letter whether the petition has been denied or approved. In the case of an appropriate petition, an order classifying the device into Class I or II will be published in the FEDERAL REGISTER.

Petitions for reclassification should be sent directly to the Food and Drug Administration, Document Mail Center (HFZ-401), 5600 Fishers Lane, Rockville, Maryland 20857. The outside of the envelope should be clearly marked with the section of the law under which the petition is being submitted: for example, "513(e) Petition" or other applicable section. The petition and five copies should be submitted on standard size paper.

After final classification is completed, all types of petitions submitted to reclassify a device should include the following information:

- o generic group of devices to which the petition is applicable:
- o specific action that is being requested by the petition (e.g., "It is requested that devices(s) be reclassified from Class III to Class II."):
- o completed supplementary data sheets:*
- o completed classification questionnaire:*
- o full statement of reasons and supporting data demonstrating why the device should not be continued in its present classification and how the proposed reclassification will provide reasonable assurance of safety and effectiveness: and
- o a summary of new information used to support the petition, if that petition is based on new information under Sections 513(e), 514(b), or 515(b) of the Act.

For information and guidance on classification and reclassification, contact:

o Office of Device Evaluation
Investigational Device Exemption Staff, HFZ-403
(301) 427-8162

o Division of Small Manufacturers Assistance, HFZ-220
(301) 443-6597 or 800 638-2041

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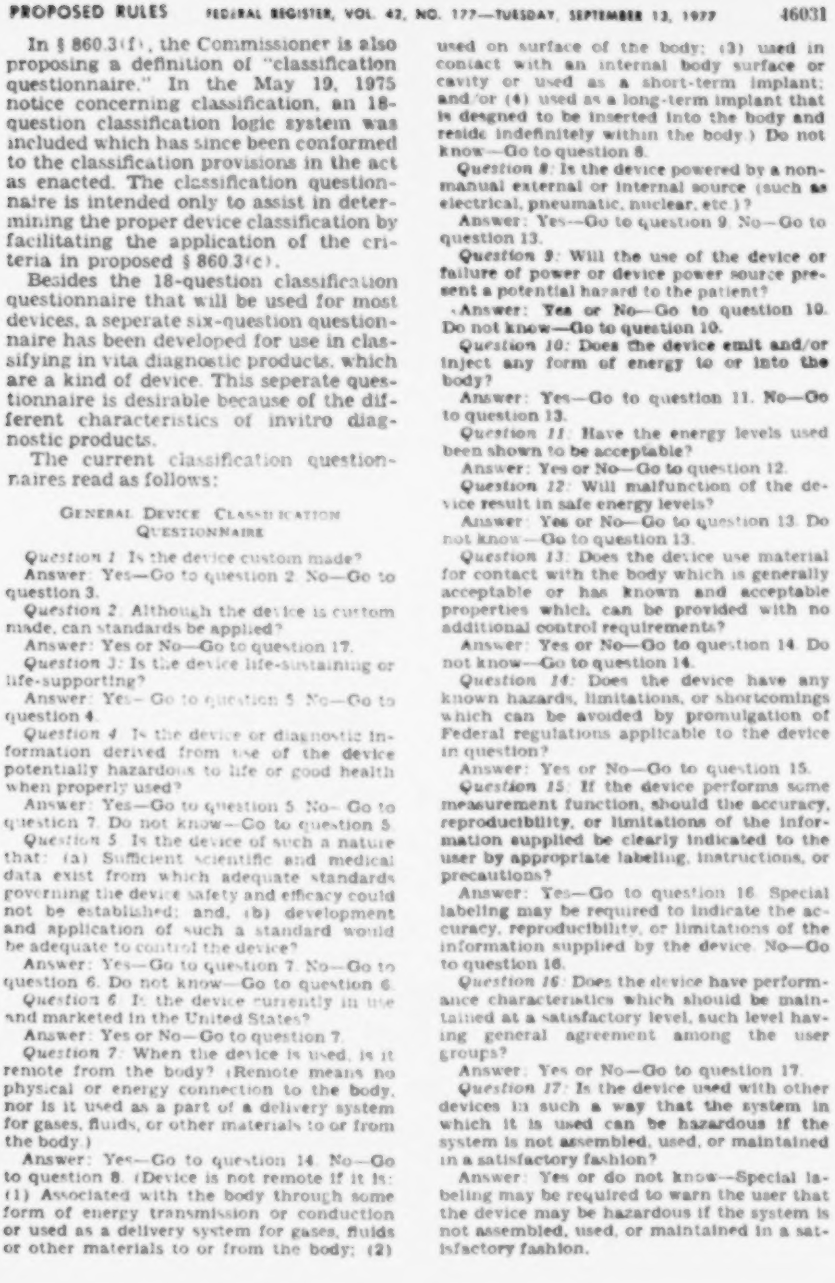
*See following pages for classification questionnaire form and supplementary data sheets.

CLASSIFICATION QUESTIONNAIRE



PROPOSED RULES FEDERAL REGISTER, VOL. 42, NO. 177—TUESDAY, SEPTEMBER 13, 1977 46031

In § 860.3(f), the Commissioner is also proposing a definition of "classification questionnaire." In the May 19, 1975 notice concerning classification, an 18-question classification logic system was included which has since been conformed to the classification provisions in the act as enacted. The classification questionnaire is intended only to assist in determining the proper device classification by facilitating the application of the criteria in proposed § 860.3(c).

Besides the 18-question classification questionnaire that will be used for most devices, a seperate six-question questionnaire has been developed for use in classifying in vita diagnostic products, which are a kind of device. This seperate questionnaire is desirable because of the different characteristics of invitro diagnostic products.

The current classification questionnaires read as follows:

GENERAL DEVICE CLASSIFICATION QUESTIONNAIRE

Question 1: Is the device custom made?

Answer: Yes—Go to question 2. No—Go to question 3.

Question 2: Although the device is custom made, can standards be applied?

Answer: Yes or No—Go to question 17.

Question 3: Is the device life-sustaining or life-supporting?

Answer: Yes—Go to question 5. No—Go to question 4.

Question 4: Is the device or diagnostic information derived from use of the device potentially hazardous to life or good health when properly used?

Answer: Yes—Go to question 5. No—Go to question 7. Do not know—Go to question 5.

Question 5: Is the device of such a nature that: (a) Sufficient scientific and medical data exist from which adequate standards governing the device safety and efficacy could not be established; and, (b) development and application of such a standard would be adequate to control the device?

Answer: Yes—Go to question 7. No—Go to question 6. Do not know—Go to question 6.

Question 6: Is the device currently in use and marketed in the United States?

Answer: Yes or No—Go to question 7.

Question 7: When the device is used, is it remote from the body? (Remote means no physical or energy connection to the body, nor is it used as a part of a delivery system for gases, fluids, or other materials to or from the body.)

Answer: Yes—Go to question 14. No—Go to question 8. (Device is not remote if it is: (1) Associated with the body through some form of energy transmission or conduction or used as a delivery system for gases, fluids or other materials to or from the body; (2) used on surface of the body; (3) used in contact with an internal body surface or cavity or used as a short-term implant; and/or (4) used as a long-term implant that is desgned to be inserted into the body and reside indefinitely within the body.) Do not know—Go to question 8.

Question 8: Is the device powered by a non-manual external or internal source (such as electrical, pneumatic, nuclear, etc.)?

Answer: Yes—Go to question 9. No—Go to question 13.

Question 9: Will the use of the device or failure of power or device power source present a potential hazard to the patient?

Answer: Yes or No—Go to question 10. Do not know—Go to question 10.

Question 10: Does the device emit and/or inject any form of energy to or into the body?

Answer: Yes—Go to question 11. No—Go to question 13.

Question 11: Have the energy levels used been shown to be acceptable?

Answer: Yes or No—Go to question 12.

Question 12: Will malfunction of the device result in safe energy levels?

Answer: Yes or No—Go to question 13. Do not know—Go to question 13.

Question 13: Does the device use material for contact with the body which is generally acceptable or has known and acceptable properties which can be provided with no additional control requirements?

Answer: Yes or No—Go to question 14. Do not know—Go to question 14.

Question 14: Does the device have any known hazards, limitations, or shortcomings which can be avoided by promulgation of Federal regulations applicable to the device in question?

Answer: Yes or No—Go to question 15.

Question 15: If the device performs some measurement function, should the accuracy, reproducibility, or limitations of the information supplied be clearly indicated to the user by appropriate labeling, instructions, or precautions?

Answer: Yes—Go to question 16. Special labeling may be required to indicate the accuracy, reproducibility, or limitations of the information supplied by the device. No—Go to question 16.

Question 16: Does the device have performance characteristics which should be maintained at a satisfactory level, such level having general agreement among the user groups?

Answer: Yes or No—Go to question 17.

Question 17: Is the device used with other devices in such a way that the system in which it is used can be hazardous if the system is not assembled, used, or maintained in a satisfactory fashion?

Answer: Yes or do not know—Special labeling may be required to warn the user that the device may be hazardous if the system is not assembled, used, or maintained in a satisfactory fashion.

Question 18: **Is the device potentially hazardous to the fetus or the gonads when properly used?**

Answer: Yes or do not know—The device will be reviewed by the obstetrical and gynecological panel and the classifying panel jointly for further classification.

IN VITRO DIAGNOSTIC PRODUCT CLASSIFICATION QUESTIONNAIRE

Question 1: Is the in vitro diagnostic product or information derived from the use of the diagnostic product potentially hazardous to life, health, or well being when put to its intended use?

Answer: Yes or No—Go to question 2.

Question 2: Are general controls (class I), adequate to ensure the safe and effective use of the product?

Answer: Yes—Go to question 5. No—Go to question 3.

Question 3: Considering the nature and complexity of the product and available scientific and medical data, is it possible to develop a standard or set of standards to control the safety or effectiveness of the diagnostic product?

Answer: Yes—Go to question 5. No—Go to question 4.

Question 4: Can some components or characteristics of the product be adequately controlled by standards? Specify.

Answer: Yes or No—Go to question 5.

Question 5: Are there any special problems relating to the product that require special attention: (For example, special labeling requirements including areas such as warnings)? Identify the problem.

Answer: Yes—Go on to question 6.

Question 6: Does the product require some form of certification? Define.

The Commissioner is also proposing a definition of "supplemental data sheet." The supplemental data sheet has been prepared to gather together and report information relevant to the classification and reclassification of a device and is to be used by classification panels and may be used in petitions for reclassification to satisfy the requirements of proposed § 860.123(a)(3).

The classification questionnaire and supplemental data sheet may be changed from time to time as the agency gains experience in their use. Current copies may be obtained from the Classification Coordinator (HFK-400), Bureau of Medical Devices, Food and Drug Administration, 8757 Georgia Ave., Silver Spring, MD 20910.

The proposed definition of "generic type of device" is intended to identify those device products that are so similar that they can be considered the same type of device for purposes of applying the regulatory controls provided by the act. The definition of "generic type of device" is important for proposed Part 860 because actions taken on both classification and reclassification apply to all devices which are within the same generic type of device and which are substantially equivalent. This approach is necessary to enable the Commissioner to provide similar regulatory treatment for essentially identical products of different manufacturers or importers.

Confidentiality and use of data and information submitted in connection with classification and reclassification. Proposed § 860.5 governs the availability for public disclosure and the use by the Commissioner of any data and information submitted to the classification panels or the Commissioner in connection with the classification and reclassification of devices under proposed Part 860.

The policy expressed in § 860.5(c) concerning the availability for public disclosure of safety and effectiveness data submitted in connection with clasification codifies rules announced in the May 19, 1975, notice on interim medical device classification procedures and is consistent with the legislative history of the amendments (Ref. 1, at pp. 48-50).

CLASSIFICATION QUESTIONNAIRE FORM

Medical Device Classification System

Panel Member: ____________________ Date: __________

Device: ______________________________

Use Categories: ☐ Diagnostic ☐ Monitoring ☐ Prosthetic ☐ Surgical ☐ Therapeutic ☐ Other

Regulatory Level: I. General Controls
II. Performance Standards
III. Premarket Approval

Specific device problems: Yes No

Classification System	Yes	No	Do Not Know	Regulatory Level	Question Scheme
1. Custom Made?					Yes--2 No--3
2. Custom Made: Standard?					Yes No 17
3. Life-sustaining?					Yes--5 No--4
4. Potentially hazardous to life, good health					Yes DNK } 5 No--7
5. (a) Can standards be developed now; and (b) would standard be adequate?					Yes--7 No DNK --6
6. Marketed in U.S.?					Yes No } 7
7. Remote from body?					Yes--14 No DNK } 8
8. Powered?					Yes--9 No--13
9. Failure of power: hazardous to patient?					Yes DNK No } 10
10. Introduce energy into body?					Yes--11 No--13
11. Acceptable energy levels?					Yes No } 12
12. Safe energy levels if malfunction?					Yes No DNK } 13
13. Material regarded as safe without standard:					Yes No DNK } 14
14. Proscriptions needed? limitation, hazards, difficulties, problems					Yes No } 15
15. Labeling, instructions or precautions on measurement function?					Yes No } 16
16. Performance Standards?					Yes No } 17
17. Special safety systems considerations?					Yes No DNK } 18
18. Potentially hazardous to fetus and/or gonads					Yes DNK } To Ob-Gyn Panel
Low Density Coding Form					

Supplementary Data Sheet
Summary of Reasons for Classification

1. Device Name ______________________________

2. Classification Panel ______________________________

3. Is device an implant? ______________________________

4. Indications for use prescribed, recommended, or suggested in the device's labeling that were considered by the panel ______________________________

____

5. Identification of any risks to health presented by device

General ______________________________

____

____

Specific Hazards to Health	Characteristic or Feature of Device Associated with Hazard
a. ____________	a. ____________
b. ____________	b. ____________
c. ____________	c. ____________
d. ____________	d. ____________

6. Recommended panel classification and priority

Classification	Priority (Class II or III Only)
____________	____________

7. If device is an implant, or is life-sustaining or life-supporting, and has been classified in a category other than Class III, explain fully reasons for the lower classification with supporting documentation and data

____

____

____

____

8. Summary of data including clinical experience or judgment upon which classification recommendation is based

____

____

____

9. Identification of any needed restrictions on the use of the device

____

____

____

10. If device is in Class I, recommend whether FDA should exempt it from:

	Justification/COMMENTS
a. Registration	a. ________________
b. Records and Reports	b. ________________
c. Good Manufacturing Practice	c. ________________

11. Existing standards applicable to the device, device subassemblies (components), or device materials (parts and accessories)

____

____

____

____

CLASSIFIED DEVICES BY CLASSIFICATION REGULATION

The list below shows final classifications of devices, their classes, and their regulation section numbers in the Code of Federal Regulations. Devices are grouped by their respective classification panels; the first list below starting with those in anesthesiology, and the last list with those in radiology. The asterisked items indicate the final classification is different from that originally proposed for the device.

A list of exemptions for certain Class I devices can be found in the chapter on "Premarket Notification."

Through the reclassification process, the class of some of these devices may have been changed since these regulations became effective. If you have questions about reclassification, refer them to the Division of Small Manufacturers Assistance (DSMA).

DSMA's phone number is 800 638-2041 or (301) 443-6597.

ANESTHESIOLOGY

FR July 16, 1982

Diagnostic Devices

Section	Device	Class
868.1030	Manual algesimeter	I
868.1040	Powered algesimeter	II
868.1075	Argon gas analyzer	II
868.1100	Arterial blood sampling kit	II
868.1120	Indwelling blood oxyhemoglobin concentration analyzer	III
868.1150	Indwelling blood carbon dioxide partial pressure (P_{CO_2}) analyzer	III
868.1170	Indwelling blood hydrogen ion concentration (pH) analyzer	III
868.1200	Indwelling blood oxygen partial pressure (P_{O_2}) analyzer	III
868.1400	Carbon dioxide gas analyzer	II
868.1430	Carbon monoxide gas analyzer	II
868.1500	Enflurane gas analyzer	II
868.1575	Gas collection vessel	II
868.1620	Halothane gas analyzer	II
868.1640	Helium gas analyzer	II
868.1670	Neon gas analyzer	II
868.1690	Nitrogen gas analyzer	II
868.1700	Nitrous oxide gas analyzer	II
868.1720	Oxygen gas analyzer	II
868.1730	Oxygen uptake computer	II
868.1750	Pressure plethysmograph	II
868.1760	Volume plethysmograph	II

868.1780	Inspiratory airway pressure meter	II
868.1800	Rhinoanemometer	II
868.1840	Diagnostic spirometer	II
868.1850	Monitoring spirometer	II
868.1860	Peak-flow meter for spirometry	II
868.1870	Gas volume calibrator	II
868.1880	Pulmonary-function data calculator	II
868.1890	Predictive pulmonary-function value calculator	II
868.1900	Diagnostic pulmonary-function interpretation calculator	II
868.1910	Esophageal stethoscope	I
868.1920	Esophageal stethoscope with electrical conductors	II
868.1930	Stethoscope head	I
868.1965	Switching valve (ploss)	I
868.1975	Water vapor analyzer	II

Monitoring Devices

Section	Device	Class
868.2025	Ultrasonic air embolism monitor	II
868.2300	Bourdon gauge flowmeter	II
868.2320	Uncompensated thorpe tube flowmeter	II
868.2340	Compensated thorpe tube flowmeter	II
868.2350	Gas calibration flowmeter	II
868.2375	Breathing frequency monitor	II
868.2450	Lung water monitor	III
868.2500	Cutaneous oxygen monitor	II, III
868.2550	Pneumotachometer	II
868.2600	Airway pressure monitor	II
868.2610	Gas pressure gauge	II
868.2620	Gas pressure calibrator	II
868.2700	Pressure regulator	II
868.2775	Electrical peripheral nerve stimulator	II
868.2875	Differential pressure transducer	II
868.2885	Gas flow transducer	II
868.2900	Gas pressure transducer	II

Therapeutic Devices

Section	Device	Class
868.5090	Emergency airway needle	II
868.5100	Nasopharyngeal airway	II
868.5110	Oropharyngeal airway	II
868.5120	Anesthesia conduction catheter	II
868.5130	Anesthesia conduction filter	II
868.5140	Anesthesia conduction kit	II
868.5150	Anesthesia conduction needle	II

868.5160	Gas machine for anesthesia or analagesia	II
868.5170	Laryngotracheal topical anesthesia applicator	II
868.5180	Rocking bed	II
868.5220	Blow bottle	I
868.5240	Anesthesia breathing circuit	II
868.5250	Breathing circuit circulator	II
868.5260	Breathing circuit bacterial filter	II
868.5270	Breathing system heater	II
868.5280	Breathing tube support	I
868.5300	Carbon dioxide absorbent	II
868.5310	Carbon dioxide absorber	II
868.5320	Reservoir bag	II
868.5330	Breathing gas mixer	II
868.5340	Nasal oxygen cannula	I
868.5350	Nasal oxygen catheter	I
868.5365	Posture chair for cardiac or pulmonary treatment	I
868.5375	Heat and moisture condenser (artificial nose)	II
868.5400	Electroanesthesia apparatus	III
868.5420	Ether hook	I
868.5430	Gas-scavenging apparatus	II
868.5440	Portable oxygen generator	II
868.5450	Respiratory gas humidifier	II
868.5460	Therapeutic humidifier for home use	II
868.5470	Hyperbaric chamber	II
868.5530	Flexible laryngoscope	II
868.5540	Rigid laryngoscope	II
868.5550	Anesthestic gas mask	II
868.5560	Gas mask head strap	I
868.5570	Nonrebreathing mask	II
868.5580	Oxygen mask	II
868.5590	Scavenging mask	II
868.5600	Venturi mask	II
868.5610	Membrane lung for long-term pulmonary support	III
868.5620	Breathing mouthpiece	I
868.5630	Nebulizer	II
868.5640	Medicinal nonventilatory nebulizer (atomizer)	I
868.5650	Esophageal obturator	II
868.5655	Portable liquid oxygen unit	II
868.5665	Powered percussor	II
868.5675	Rebreathing device	I
868.5690	Incentive spirometer	II
868.5700	Nonpowered oxygen tent	I
868.5710	Electrically powered oxygen tent	II
868.5720	Bronchial tube	II
868.5730	Tracheal tube	II
868.5740	Tracheal/bronchial differential ventilation tube	II
868.5750	Inflatable tracheal tube cuff	II
868.5760	Cuff spreader	I
868.5770	Tracheal tube fixation device	II
868.5780	Tube introduction forceps	II
868.5790	Tracheal tube stylet	II
868.5810	Airway connector	II
868.5820	Dental protector	II
868.5830	Autotransfusion apparatus	II

868.5860	Pressure tubing and accessories	II
868.5870	Nonrebreathing valve	II
868.5880	Anesthetic vaporizer	II
868.5895	Continuous ventilator	II
868.5905	Noncontinuous ventilator (PPB)	II
868.5915	Manual emergency ventilator	II
868.5925	Powered emergency ventilator	II
868.5935	External negative pressure ventilator	II
868.5955	Intermittent mandatory ventilation attachment	II
868.5965	Positive end expiratory pressure breathing attachment	II
868.5975	Ventilator tubing	II
868.5995	Tee drain (water trap)	II

Miscellaneous

Section	Device	Class
868.6100	Anesthetic cabinet. table. or tray	I
868.6175	Cardiopulmonary emergency cart	I
868.6225	Nose clip	I
868.6250	Portable air compressor	II
868.6400	Calibration gas	II
868.6700	Anesthesia stool	I
868.6810	Tracheobronchial suction catheter	I
868.6820	Patient position support	II
868.6885	Medical gas yoke assembly	II

CARDIOVASCULAR

FR February 5, 1980

Diagnostic Devices

Section	Device	Class
870.1025	Arrhythmia detector and alarm	III
870.1100	Blood pressure alarm	II
870.1110	Blood pressure computer	II
870.1120	Blood pressure cuff	II
870.1130	Noninvasive blood pressure measurement system	II
870.1140	Venous blood pressure manometer	II
870.1200	Diagnostic intravascular catheter	II
870.1210	Continuous flush catheter	II
870.1220	Electrode recording catheter or electrode recording probe	II
870.1230	Fiberoptic oximeter catheter	II
870.1240	Flow-directed catheter	II

870.1250	Percutaneous catheter	II
870.1270	Intracavitary phonocatheter system	II
870.1280	Steerable catheter	II
870.1290	Steerable catheter control system	II
870.1300	Catheter cannula	II
870.1310	Vessel dilator for percutaneous catheterization	II
870.1330	Catheter guide wire	II
870.1340	Catheter introducer	II
870.1350	Catheter balloon repair kit	III
870.1360	Trace microsphere	III
870.1370	Catheter tip occluder	II
870.1380	Catheter stylet	II
870.1390	Trocar	II
870.1425	Programmable diagnostic computer	II
870.1435	Single-function, preprogrammed diagnostic computer	II
870.1450	Densitometer	II
870.1650	Angiographic injector and syringe	II
870.1660	Indicator injector	II
870.1670	Syringe actuator for an injector	II
870.1750	External programmable pacemaker pulse generator	II
870.1800	Withdrawal-infusion pump	II
870.1875	Stethoscope	I, II
870.1915	Thermodilution probe	II

Monitoring Devices

Section	Device	Class
870.2050	Biopotential amplifier and signal conditioner	II
870.2060	Transducer signal amplifier and signal conditioner	II
870.2100	Cardiovascular blood flowmeter	II
870.2120	Extravascular blood flow probe	II
870.2300	Cardiac monitor (including cardiotachometer and rate alarm)	II
870.2310	Apex cardiograph (vibrocardiograph)	II
870.2320	Ballistocardiograph	II
870.2330	Echocardiograph	II
870.2340	Electrocardiograph	II
870.2350	Electrocardiograph lead switching adaptor	II
870.2360	Electrocardiograph electrode	II
870.2370	Electrocardiograph surface electrode tester	II
870.2390	Phonocardiograph	II
870.2400	Vectorcardiograph	II
870.2450	Medical cathode-ray tube display	II
870.2600	Signal isolation system	II
870.2620	Line isolation monitor	II
870.2640	Portable leakage current alarm	II
870.2675	Oscillometer	II
870.2700	Oximeter	II
870.2710	Ear oximeter	II
870.2750	Impedance phlebograph	II
870.2770	Impedance plethysmograph	II

870.2780	Hydraulic, pneumatic, or photoelectric plethysmograph	II
870.2800	Medical magnetic tape recorder	II
870.2810	Paper chart recorder	II
870.2840	Apex cardidographic transducer	II
870.2850	Extravascular blood pressure transducer	II
870.2860	Heart sound transducer	II
870.2870	Catheter tip pressure transducer	II
870.2880	Ultrasonic transducer	II
870.2890	Vessel occlusion transducer	II
870.2900	Patient transducer and electrode cable (including connector)	II
870.2910	Radiofrequency physiological signal transmitters and receivers	II
870.2920	Telephone electrocardiograph transmitters and receivers	II

Prosthetic Devices

Section	Device	Class
870.3250	Vascular clip	II
870.3260	Vena cava clip	II
870.3300	Arterial embolization device	III
870.3375	Cardiovascular intravascular filter	III
870.3450	Vascular graft prosthesis of less than 6 mm diameter	III
870.3460	Vascular graft prosthesis of 6 mm and greater diameter	II
870.3470	Intracardiac patch or pledget made of polypropylene, polyethylene terephthalate, or polytetrafluoroethylene	II
870.3535	Intra-aortic balloon and control system	III
870.3545	Ventricular bypass (assist) devices	III
870.3600	External pacemaker pulse generator	III
870.3610	Implantable pacemaker pulse generator	III
870.3620	Pacemaker lead adaptor	III
870.3630	Pacemaker generator function analyzer	II
870.3640	Indirect pacemaker generator function analyzer	II
870.3650	Pacemaker polymeric mesh bag	II
870.3670	Pacemaker charger	II
870.3680	Cardiovascular permanent and temporary pacemaker electrode	II, III
870.3690	Pacemaker test magnet	II
870.3700	Pacemaker programmers	III
870.3710	Pacemaker repair or replacement material	III
870.3720	Pacemaker electrode function tester	II
870.3730	Pacemaker service tools	I
870.3800	Annuloplasty ring	III
870.3850	Cartoid sinus nerve stimulator	III
870.3925	Replacement heart valve	III
870.3935	Prosthesis heart valve holder	II
870.3945	Prosthesis heart valve sizer	II

Surgical Devices

Section	Device	Class
870.4075	Endomyocardial biopsy device	II
870.4200	Cardiopulmonary bypass accessory equipment	I
870.4205	Cardiopulmonary bypass bubble detector	II
870.4210	Cardiopulmonary bypass vascular catheter, cannula, or tubing	II
870.4220	Cardiopulmonary bypass heart-lung machine console	II
870.4230	Cardiopulmonary bypass defoamer	III
870.4240	Cardiopulmonary bypass heat exchanger	II
870.4250	Cardiopulmonary bypass temperature controller	II
870.4260	Cardiopulmonary bypass arterial line blood filter	III
870.4270	Cardiopulmonary bypass cardiotomy suction line blood filter	II
870.4280	Cardiopulmonary pre-bypass filter	II
870.4290	Cardiopulmonary bypass adaptor, stopcock, manifold, or fitting	II
870.4300	Cardiopulmonary bypass gas control unit	II
870.4310	Cardiopulmonary bypass coronary pressure gauge	II
870.4320	Cardiopulmonary bypass pulsatile flow generator	III
870.4330	Cardiopulmonary bypass on-line blood gas monitor	II
870.4340	Cardiopulmonary bypass level sensing monitor and/or control	II
870.4350	Cardiopulmonary bypass oxygenator	III
870.4360	Nonroller type cardiopulmonary bypass blood pump	III
870.4370	Roller-type cardiopulmonary bypass blood pump	II
870.4380	Cardiopulmonary bypass pump speed control	II
870.4390	Cardiopulmonary bypass pump tubing	II
870.4400	Cardiopulmonary bypass blood reservoir	II
870.4410	Cardiopulmonary bypass in-line blood gas sensor	II
870.4420	Cardiopulmonary bypass cardiotomy return sucker	II
870.4430	Cardiopulmonary bypass intracardiac suction control	II
870.4450	Vascular clamp	II
870.4475	Surgical vessel dilator	II
870.4500	Cardiovascular surgical instruments	I
870.4875	Intraluminal artery stripper	II
870.4885	External vein stripper	II

Therapeutic Devices

Section	Device	Class
870.5050	Patient care suction apparatus	II
870.5150	Embolectomy catheter	II
870.5175	Septostomy catheter	II
870.5200	External cardiac compressor	III
870.5225	External counter-pulsating device	III
870.5300	DC-defibrillator (including paddles)	II, III
870.5325	Defibrillator tester	II
870.5550	External transcutaneous cardiac pacemaker (noninvasive)	III

870.5800	Compressible limb sleeve	II
870.5900	Thermal regulating system	II
870.5925	Automatic rotating tourniquet	II

CLINICAL CHEMISTRY, TOXICOLOGY

FR May 1, 1987

Clinical Chemistry Test Systems

Section	Device	Class
862.1020	Acid Phosphatase (total or prostatic test system)	II
862.1025	Adrenocorticotropic hormone (ACTH) test system	II
862.1030	Alanine amino transferase (ALT/SGPT) test system*	I
862.1035	Albumin test system	II
862.1040	Aldolase test system*	I
862.1045	Aldosterone test system	II
862.1050	Alkaline phosphatase or isoenzymes test system	II
862.1060	Delta-aminolevulinic acid test system*	I
862.1065	Ammonia test system*	I
862.1070	Amylase test system	II
862.1075	Androstenedione test system*	I
862.1080	Androsterone test system*	I
862.1085	Angiotensin I and renin test system	II
862.1090	Angiotensin converting enzyme test (A.C.E) system	II
862.1095	Ascorbic acid test system*	I
862.1100	Aspartate amino transferase (AST/SGOT) test system	II
862.1110	Bilirubin (total or direct) test system	II
862.1115	Urinary bilirubin and its conjugates (nonquantitative) test system*	I
862.1120	Blood gases ($P_{c0}2P_{0}2$) and blood pH test system	II
862.1130	Blood volume test system*	I
862.1135	C-Peptides of pro-insulin test system*	I
862.1140	Calcitonin test system	II
862.1145	Calcium test system	II
862.1150	Calibrator	II
862.1155	Human chorionic gonadotropin (HCG) test system	II, III
862.1160	Bicarbonate/carbon dioxide test system	II
862.1165	Catecholamines (total) test system*	I
862.1170	Chloride test system	II
862.1175	Cholesterol (total) test system*	I
862.1177	Cholylglycine test system	II
862.1180	Chymotrypsin test system*	I
862.1185	Compound S (11-deoxycortisol) test system*	I
862.1187	Conjugated sulfolithocholic acid (SLCG) test system	II
862.1190	Copper test system*	I
862.1195	Corticoids test system*	I

862.1200	Corticosterone test system*	I
862.1205	Cortisol (hydrocortisone and hydroxycorticosterone) test system	II
862.1210	Creatine test system*	I
862.1215	Creatine phosphokinase/creatine kinase or isoenzymes test system	II
862.1225	Creatinine test system	II
862.1230	Cyclic AMP test system	II
862.1240	Cystine test system*	I
862.1245	Dehydroepiandrosterone (free and sulfate) test system*	I
862.1250	Desoxycorticosterone test system*	I
862.1255	2.3-Diphosphoglyceric acid test system*	I
862.1260	Estradiol test system*	I
862.1265	Estriol test system*	I
862.1270	Estrogens (total in pregnancy) test system*	I
862.1275	Estrogens (total, nonpregnancy) test system*	I
862.1280	Estrone test system*	I
862.1285	Etiocholanolone test system*	I
862.1290	Fatty acids test system*	I
862.1295	Folic acid test system	II
862.1300	Follicle-stimulating hormone test system*	I
862.1305	Formiminoglutamic acid (FIGLU) test system*	I
862.1310	Galactose test system*	I
862.1315	Galactose-1 phosphate uridyl transferase test system	II
862.1320	Gastric acidity test system*	I
862.1325	Gastrin test system*	I
862.1330	Globulin test system*	I
862.1335	Glucagon test system*	I
862.1340	Urinary glucose (nonquantitative) test system	II
862.1345	Glucose test system	II
862.1360	Gamma-glutamyl transpeptidase and isoenzymes test system*	I
862.1365	Glutathione test system*	I
862.1370	Human growth hormone test system*	I
862.1375	Histidine test system*	I
862.1377	Urinary homocystine (nonquantitative) test system	II
862.1380	Hydroxybutyric dehydrogenase test system*	I
862.1385	17-Hydroxycortico-steroids (17-ketogenic steriods) test system*	I
862.1390	5-Hydroxyindole acetic acid/serotonin test system*	I
862.1395	17-Hydroxyprogesterone test system*	I
862.1400	Hydroxyproline test system*	I
862.1405	Immunoreactive insulin test system*	I
862.1410	Iron (non-heme) test system*	I
862.1415	Iron-binding capacity test system*	I
862.1420	Isocitric dehydrogenase test system*	I
862.1430	17-Ketosteroids test system*	I
862.1435	Ketones (non-quantitative) test system*	I
862.1440	Lactate dehydrogenase test system	II
862.1445	Lactate dehydrogenase isoenzymes test system	II
862.1450	Lactic acid test system*	I
862.1455	Lecithin/sphingomyelin ratio in amniotic fluid test system	II
862.1460	Leucine aminopeptidase test system*	I
862.1465	Lipase test system*	I
862.1470	Lipid (total) test system*	I

862.1475	Lipoprotein test system*	I
862.1485	Luteinizing hormone test system*	I
862.1490	Lysozyme (muramidase) test system*	I
862.1495	Magnesium test system*	I
862.1500	Malic dehydrogenase test system*	I
862.1505	Mucopolysaccharides (nonquantitative) test system*	I
862.1509	Methylmalonic acid (nonquantitative) test system	II
862.1510	Nitrite (nonquantitative) test system*	I
862.1515	Nitrogen (aminonitrogen) test system*	I
862.1520	5'-Nucleotidase test system*	I
862.1530	Plasma oncometry test system*	I
862.1535	Ornithine carbamyl transferase test system*	I
862.1540	Osmolality test system*	I
862.1542	Oxalate test system	I
862.1545	Parathyroid hormone test system	II
862.1550	Urinary pH (nonquantitative) test system*	I
862.1555	Phenylalanine test system	II
862.1560	Urinary phenylketones (nonquantitative) test system*	I
862.1565	6-Phosphogluconate dehydrogenase test system*	I
862.1570	Phosphohexose isomerase test system*	I
862.1575	Phospholipid test system*	I
862.1580	Phosphorus (inorganic) test system*	I
862.1585	Human placental lactogen test system	II
862.1590	Porphobilinogen test system*	I
862.1595	Porphyrins test system*	I
862.1600	Potassium test system	II
862.1605	Pregnanediol test system*	I
862.1610	Pregnanetriol test system*	I
862.1615	Pregnenolone test system*	I
862.1620	Progesterone test system*	I
862.1625	Prolactin (lactogen) test system*	I
862.1630	Protein (fractionation) test system*	I
862.1635	Total protein test system	II
862.1640	Protein-bound iodine test system*	I
862.1645	Urinary protein or albumin (nonquantitative) test system*	I
862.1650	Pyruvate kinase test system*	I
862.1655	Pyruvic acid test system*	I
862.1660	Quality control material (assayed and unassayed)	I
862.1665	Sodium test system	II
862.1670	Sorbitol dehydrogenase test system*	I
862.1675	Blood specimen collection device	II
862.1680	Testosterone test system*	I
862.1685	Thyroxine-binding globulin test system	II
862.1690	Thyroid-stimulating hormone test system	II
862.1695	Free thyroxine test system	II
862.1700	Total thyroxine test system	II
862.1705	Triglyceride test system*	I
862.1710	Total triiodothyronine test system	II
862.1715	Triiodothyronine uptake test system	II
862.1720	Triose phosphate isomerase test system*	I
862.1725	Trypsin test system*	I
862.1730	Free tryosine test system*	I
862.1770	Urea nitrogen test	II
862.1775	Uric acid test system*	I

862.1780	Urinary calculi (stone) test system*	I
862.1785	Urinary urbilinogen (nonquantitative) test system*	I
862.1790	Uroporphyrin test system*	I
862.1795	Vanilmandelic acid test system*	I
862.1805	Vitamin A test system*	I
862.1810	Vitamin B_{12} test system	II
862.1815	Vitamin E test system*	I
862.1820	Xylose test system*	I

Clinical Laboratory Instruments

Section	Device	Class
862.2050	General purpose laboratory equipment labeled or promoted for a specific medical use	I
862.2100	Calculator/data processing module for clinical use	I
862.2140	Centrifugal chemistry analyzer for clinical use	I
862.2150	Continuous flow sequential multiple chemistry analyzer for clinical use	I
862.2160	Discrete photometric chemistry analyzer for clinical use	I
862.2170	Micro chemistry analyzer for clinical use	I
862.2230	Chromatographic separation material for clinical use	I
862.2250	Gas liquid chromatography system for clinical use	I
862.2260	High-pressure liquid chromatography system for clinical use	I
862.2270	Thin-layer chromatography system	I
862.2300	Colorimeter, photometer, or spectrophotometer for clinical use	I
862.2310	Clinical sample concentrator	I
862.2320	Beta or gamma counter for clinical use	I
862.2400	Densitometer/scanner (integrating, reflectance, TLC or radiochromatogram) for clinical use	I
862.2485	Electrophoresis apparatus for clinical use	I
862.2500	Enzyme analyzer for clinical use	I
862.2540	Flame emission photometer for clinical use	I
862.2560	Fluorometer for clinical use	I
862.2680	Microtitrator for clinical use	I
862.2700	Nephelometer for clinical use	I
862.2720	Plasma oncometer for clinical use	I
862.2730	Osmometer for clinical use	I
862.2750	Pipetting and diluting system for clinical use	I
862.2800	Refractometer for clinical use	I
862.2850	Atomic absorption spectrophotometer for clinical use	I
862.2860	Mass spectrometer for clinical use	I
862.2900	Automated urinalysis system	I
862.2920	Plasma viscometer for clinical use	I

Clinical Toxicology Test System

Section	Device	Class
862.3030	Acetaminophen test system	II
862.3035	Amikacin test system	II
862.3040	Alcohol test system	II
862.3050	Breath-alcohol test system	I
862.3100	Amphetamine test system	II
862.3110	Antimony test system*	I
862.3120	Arsenic test system*	I
862.3150	Barbiturate test system*	II
862.3170	Benzodiazepine test system	II
862.3200	Clinical toxicology calibrator	II
862.3220	Carbon monoxide test system*	I
862.3240	Cholinesterase test system*	I
862.3250	Cocaine and cocaine metabolite test system	II
862.3270	Codeine test system	II
862.3280	Clinical toxicology control material	I
862.3300	Digitoxin test system	II
862.3320	Digoxin test system	II
862.3350	Diphenylhydantoin test system	II
862.3380	Ethosuximide test system	II
862.3450	Gentamicin test system	II
862.3520	Kanamycin test system	II
862.3550	Lead test system	II
862.3555	Lidocaine test system	II
862.3560	Lithium test system	II
862.3580	Lysergic acid diethylamide (LSD) test system	II
862.3600	Mercury test system*	I
862.3610	Methamphetamine test system	II
862.3620	Methadone test system	II
862.3630	Methaqualone test system	II
862.3640	Morphine test system	II
862.3645	Neuroleptic drugs radioreceptor assay test system	II
862.3650	Opiate test system	II
862.3660	Phenobarbital test system	II
862.3670	Phenothiazine test system	II
862.3680	Primidone test system	II
862.3700	Propoxyphene test system	II
862.3750	Quinine test system	I
862.3830	Salicylate test system	II
862.3850	Sulfonamide test system	I
862.3870	Cannabinoid test system	II
862.3880	Theophylline test system	II
862.3900	Tobramycin test system	II
862.3910	Tricyclic antidepressant drugs test system	II
862.3950	Vancomycin test system	II

DENTAL

FR August 12, 1987

Diagnostic Devices

Section	Device	Class
872.1500	Gingival fluid measurer	I
872.1720	Pulp tester	II
872.1730	Electrode gel for pulp tester	I
872.1740	Caries detection device	II
872.1800	Extraoral source X-ray system	II
872.1810	Intraoral source X-ray system	II
872.1820	Dental X-ray exposure alignment device	I
872.1830	Cephalometer	II
872.1840	Dental X-ray position indicating device	II
872.1850	Lead-lined position indicator	II
872.1905	Dental X-ray film holder	I

Prosthetic Devices

Section	Device	Class
872.3050	Amalgam alloy	II
872.3060	Gold based alloys and precious metal alloys for clinical use	II
	Gold based alloy for clinical use	
	Precious metal alloy for clinical use	
872.3080	Mercury and alloy dispenser	I
872.3100	AC-powered dental amalgamator	
872.3110	Dental amalgam capsule	I
872.3130	Preformed anchor	I
872.3140	Resin applicator	I
872.3150	Articulator	I
872.3165	Precision attachment	I
	Precision attachment	
	Preformed bar	
872.3200	Resin tooth bonding agent	II
872.3220	Facebow	I
872.3240	Dental bur	I
872.3250	Calcium hydroxide cavity liner	II
872.3260	Cavity varnish	II
872.3275	Dental cement	I, II
	Dental cement	
	Zinc oxide eugenol	
872.3285	Preformed clasp	I
	Preformed clasp	
	Preformed wire clasp	

872.3300	Hydrophilic resin coating for dentures	II
872.3310	Coating material for resin fillings	II
872.3330	Preformed crown	I
872.3350	Gold or stainless steel cusp	I
872.3360	Preformed cusp	I
872.3400	Karaya and sodium borate with or without acacia denture adhesive	I, III
	Acacia and karaya with sodium borate denture adhesive	
	Karaya with sodium borate denture adhesive	
872.3410	Ethylene oxide homopolymer and/or carboxymethylcellulose sodium denture adhesive	I
	Carboxymethylcellulose sodium (40 to 100%) denture adhesive	
	Carboxymethylcellulose sodium (32%) and ethylene oxide homopolymer (13%) denture adhesive	
	Carboxymethylcellulose sodium (49%) and ethylene oxide homopolymer (21%) denture adhesive	
872.3420	Carboxymethylcellulose sodium and cationic polyacrylamide polymer denture adhesive	III
872.3450	Ethylene oxide homopolymer and/or karaya denture adhesive	I
	Karaya denture adhesive	
	Karaya and ethylene oxide homopolymer denture adhesive	
872.3480	Polyacrylamide polymer (modified cationic) denture adhesive	III
872.3490	Carboxymethylcellulose sodium and/or polyvinylmethylether maleic acid calcium-sodium double salt denture adhesive	I
	Polyvinylmethylether maleic acid calcium-sodium double salt denture adhesive	
	Polyvinylmethylether maleic acid calcium-sodium double salt and carboxymethylcellulose sodium denture adhesive	
872.3500	Polyvinylmethylether maleic anhydride (PVM-MA), acid copolymer, and carboxymethylcellulose sodium (NACMC) denture adhesive	III
872.3520	OTC denture cleanser	I
872.3530	Mechanical denture cleaner	
872.3540	OTC denture cushion or pad	I, III
	OTC denture cushion	
	OTC denture pad	
872.3560	OTC denture reliner	III
872.3570	OTC denture repair kit	III
872.3580	Preformed gold denture tooth	I
872.3590	Preformed plastic denture tooth	II
872.3600	Partially fabricated denture kit	III
872.3640	Endosseous implant	III
872.3645	Subperiosteal implant material	II
	Titanium subperiosteal implant material	
	Cobalt chrome molybdenum subperiosteal implant material	
872.3660	Impression material	II
872.3670	Resin impression tray material	I
872.3680	Polytetrafluoroethylene (PTFE) vitreous carbon material	II
872.3690	Tooth shade resin material	II
872.3700	Dental mercury	I
872.3710	Base metal alloy	II
872.3730	Pantograph	I
872.3740	Retentive and splinting pin	I
872.3750	Bracket adhesive resin and tooth conditioner	II

872.3760	Denture relining, repairing, or rebasing resin	II
872.3765	Pit and fissure sealant and conditioner	II
872.3770	Temporary crown and bridge resin	II
872.3810	Root canal post	I
872.3820	Root canal filling resin	II, III
872.3830	Endodontic paper point	I
872.3840	Endodontic silver point	I
872.3850	Gutta percha	I
872.3890	Endodontic stabilizing splint	II
872.3900	Posterior artificial tooth with a metal insert	I
872.3910	Backing and facing for an artificial tooth	I
872.3920	Porcelain tooth	II
872.3930	Tricalcium phosphate granules for dental bone repair	III

Surgical Devices

Section	Device	Class
872.4120	Bone cutting instruments and accessories	II
	Manual bone drill and wire driver	
	Powered bone drill	
	Rotary bone cutting handpiece	
	AC-powered bone saw	
872.4130	Intraoral dental drill	I
872.4200	Dental handpiece and accessories	
	Air-powered dental handpiece	
	Belt-driven dental handpiece	
	Contra angle handpiece attachment	
	Direct drive handpiece	
	Foot controller for handpiece	
	Water-powered handpiece	
872.4465	Gas-powered jet injector	II
872.4475	Spring-powered jet injector	II
872.4535	Dental diamond instrument	I
872.4565	Dental hand instrument	I
	Dental hand instrument	
	Endodontic broach	
	Dental wax carver	
	Endodontic pulp canal file	
	Hand instruments for calculus removal	
	Dental depth gauge instrument	
	Plastic dental filling instrument	
	Dental instrument handle	
	Surgical tissue scissors	
	Orthodontic band driver	
	Orthodontic band pusher	
	Orthodontic band setter	
	Orthodontic bracket aligner	
	Orthodontic pliers	
	Orthodontic ligature tucking instrument	
	Forceps for articulation paper	

	Forceps for dental dressing	
	Dental matrix band	
	Matrix retainer	
	Mouth mirror	
	Dental retractor	
	Dental retractor accessories	
	Periodontic or endodontic irrigating syringe	
	Restorative or impression material syringe	
872.4600	Intraoral ligature and wire lock	II
872.4620	Fiber optic dental light	
872.4630	Dental operating light	II
	Surgical headlight	
872.4730	Dental injecting needle	I
872.4760	Bone plate	II
872.4840	Rotary scaler	II
872.4850	Ultrasonic scaler	II
872.4880	Intraosseous fixation screw or wire	II
	Intraosseous fixation screw	
	Intraosseous fixation wire	
872.4920	Dental electrosurgical unit and accessories	II

Therapeutic Devices

Section	Device	Class
872.5410	Orthodontic appliance and accessories	I
	Preformed orthodontic band	
	Orthodontic elastic band	
	Orthodontic band material	
	Orthodontic metal bracket	
	Orthodontic wire clamp	
	Preformed orthodontic space maintainer	
	Orthodontic expansion screw retainer	
	Orthodontic spring	
	Orthodontic tube	
	Orthodontic wire	
872.5470	Orthodontic plastic bracket	II
872.5500	Extraoral orthodontic headgear	II
872.5525	Preformed tooth positioner (proposed as 872.5575)	I
872.5550	Teething ring	I, II

Miscellaneous Devices

Section	Device	Class
872.6010	Abrasive device and accessories	I
	Abrasive disk	
	Guard for an abrasive disk	

	Abrasive point	
	Polishing agent strip	
	Polishing wheel	
872.6030	Oral cavity abrasive polishing agent	I
872.6050	Saliva absorber	I
	Paper saliva absorber	
	Cotton roll	
872.6070	Ultraviolet activator for polymerization	II
872.6080	Airbrush	III
872.6100	Anesthetic warmer	I
872.6140	Articulation paper	I
872.6200	Base plate shellac	I
872.6250	Dental chair with or without operative unit	
	Dental chair with operative unit	
	Dental chair without operative unit	
872.6290	Prophylaxis cup	I
872.6300	Rubber dam and accessories	I
	Rubber dam	
	Rubber dam clamp	
	Rubber dam frame	
	Forceps for a rubber dam clamp	
872.6350	Ultraviolet detector	II
872.6390	Dental floss	I
872.6475	Heat source for bleaching teeth	
872.6510	Oral irrigation unit	
872.6570	Impression tube	I
872.6640	Dental operative unit and accessories	
	Dental operative unit	
	Saliva ejector mouthpiece	
	Oral cavity evacuator	
	Suction operative unit	
	Air or water syringe unit	
872.6650	Massaging pick or tip for oral hygiene	I
	Massaging pick	
	Rubber tip for oral hygiene	
872.6660	Porcelain powder for clinical use	II
872.6670	Silicate Protector	I
872.6710	Boiling water sterilizer	
872.6730	Endodontic dry heat sterilizer	III
872.6770	Cartridge syringe	II
872.6855	Manual toothbrush	I
872.6865	Powered toothbrush	
872.6870	Disposable fluoride tray	I
872.6880	Preformed impression tray	I
872.6890	Intraoral dental wax	I

EAR, NOSE AND THROAT

FR November 6, 1986

Diagnostic Devices

Section	Device	Class
874.1050	Audiometer	II
874.1060	Acoustic chamber for audiometric testing	I
874.1070	Short increment sensitivity index (SISI) adapter	
874.1080	Audiometer calibration set	II
874.1090	Auditory impedance tester	II
874.1100	Earphone cushion for audiometric testing	I
874.1120	Electronic noise generator for audiometric testing	II
874.1325	Electroglottograph	II
874.1500	Gustometer	I
874.1800	Air or water caloric stimulator	
	Air caloric stimulator	
	Water caloric stimulator	
874.1820	Surgical nerve stimulator/locator	II
874.1925	Toynbee diagnostic tube	I

Prosthetic Devices

Section	Device	Class
874.3300	Hearing aid	I, II
874.3310	Hearing aid calibrator and analysis system	II
874.3320	Group hearing aid or group auditory trainer	II
874.3330	Master hearing aid	II
874.3375	Battery-powered artificial larynx	I
874.3400	Tinnitus masker	III
874.3430	Middle ear mold	II
874.3450	Partial ossicular replacement prosthesis	II
	Partial ossicular replacement prosthesis	
	Porous polyethylene partial ossicular replacement prosthesis	
874.3495	Total ossicular replacement prosthesis	II
	Total ossicular replacement prosthesis	
	Porous polyethylene total ossicular replacement prosthesis	
874.3540	Prosthesis modification instrument for ossicular replacement surgery	I
874.3620	Ear, nose, and throat synthetic polymer material	II
	Ear, nose, and throat polyamide mesh or foil synthetic polymer material	
	Ear, nose, and throat porous polyethylene synthetic polymer material	
874.3695	Mandibular implant facial prosthesis	II

874.3730	Laryngeal prosthesis (Taub design)	II
874.3760	Sacculotomy tack (Cody tack)	II
874.3820	Endolymphatic shunt	II
874.3850	Endolymphatic shunt tube with valve	III
874.3880	Tympanostomy tube	II
	Tympanostomy tube	
	Porous polyethylene tympanostomy tube	
874.3930	Tympanostomy tube with semipermeable membrane	III

Surgical Devices

Section	Device	Class
874.4100	Epistaxis balloon	I
874.4140	Ear. nose. and throat bur	I
874.4175	Nasopharyngeal catheter	I
874.4250	Ear. nose. and throat electric or pneumatic surgical drill	II
874.4350	Ear. nose. and throat fiberoptic light source and carrier	II
874.4420	Ear. nose. and throat manual surgical instrument	I
	Bronchial. tracheal. or esophageal surgical instrument	
	Surgical instrument for the ear	
	Ear. nose. and throat multiple-use surgical instrument	
	Laryngeal surgical instrument	
	Pharyngeal surgical instrument	
	Nasal and paranasal sinus surgical instrument	
874.4490	Microsurgical argon laser	II. III
874.4500	Ear. nose. and throat microsurgical carbon dioxide laser	II
874.4680	Bronchoscope (flexible or rigid) and accessories	II
	Bronchoscope (flexible or rigid)	
	Ear. nose. and throat endoscopic accessory	
	Laryngeal-bronchial telescope	
874.4710	Esophagoscope (flexible or rigid) and accessories	II
874.4720	Mediastinoscope and accessories	II
874.4750	Larynogostroboscope	
	External Laryngostroboscope	
	Laryngostroboscope (patient-contacting)	
874.4760	Nasopharyngoscope (flexible or rigid) and accessories	II
874.4770	Otoscope	
868.5800 Proposed 874.4900	Tracheostomy tube and tube cuff	II
	Tracheostomy tube	
	Tracheostomy tube cuff	
868.5795 Proposed 874.4910	Tracheal tube cleaning brush	I

Therapeutic Devices

Section	Device	Class
874.5220	Ear. nose. and throat drug administration device	I
874.5300	Ear. nose. and throat examination and treatment unit	
874.5350	Suction antichoke device	III
874.5370	Tongs antichoke device	III
874.5550	Powered nasal irrigator	
874.5800	External nasal splint	I
874.5840	Antistammering device	I

GASTROENTEROLOGY-UROLOGY DEVICES

FR November 23, 1983

Diagnostic Devices

Section	Device	Class
876.1075	Gastroenterology-urology biopsy instrument	II
876.1400	Stomach pH electrode	II
876.1500	Endoscope and accessories	II
876.1620	Urodynamics measurement system	II
876.1725	Gastrointestinal motility monitoring system	II
876.1800	Urine flow or volume measuring system	II

Monitoring Devices

Section	Device	Class
876.2040	Enuresis alarm	II

Prosthetic Devices

Section	Device	Class
876.3350	Penile inflatable implant	III
876.3630	Penile rigidity implant	III
876.3750	Testicular prosthesis	III

Surgical Devices

Section	Device	Class
876.4020	Fiberoptic light ureteral catheter	II
876.4270	Colostomy rod	II
876.4300	Endoscopic electrosurgical unit and accessories	II
876.4370	Gastroenterology-urology evacuator	I, II
876.4400	Hemorrhoidal ligator	II
876.4480	Electrohydraulic lithotriptor	III
876.4500	Mechanical lithotriptor	II
876.4530	Gastroenterology-urology fiberoptic retractor	I
876.4560	Ribdam	I
876.4590	Interlocking urethral sound	II
876.4620	Ureteral stent	II
876.4650	Water jet renal stone dislodger system	II
876.4680	Ureteral stone dislodger	II
876.4730	Manual gastroenterology-urology surgical instrument and accessories	I
876.4770	Urethrotome	II
876.4890	Urological table and accessories	I, II

Therapeutic Devices

Section	Device	Class
876.5010	Biliary catheter and accessories	II
876.5030	Continent ileostomy catheter	I
876.5090	Suprapubic urological catheter and accessories	II
876.5130	Urological catheter and accessories	II
876.5160	Urological clamp for males	I
876.5210	Enema kit	I
876.5220	Colonic irrigation system	II, III
876.5250	Urine collector and accessories	I, II
876.5270	Implanted electrical urinary continence device	III
876.5280	Implanted mechanical/hydraulic urinary continence device	III
876.5320	Nonimplanted electrical continence device	II
876.5365	Esophageal dilator	II

876.5450	Rectal dilator	II
876.5470	Ureteral dilator	II
876.5520	Urethral dilator	II
876.5540	Blood access device and accessories	II. III
876.5600	Sorbent regenerated dialysate delivery system for hemodialysis	II
876.5630	Peritoneal dialysis system and accessories	II
876.5665	Water purification system for hemodialysis	II
876.5820	Hemodialysis system and accessories	I. II
876.5830	Hemodialyzer with disposable insert (Kiil type)	II
876.5860	High permeability hemodialysis system	III
876.5870	Sorbent hemoperfusion system	III
876.5880	Isolated kidney perfusion and transport system and accessories	II
876.5895	Ostomy irrigator	II
876.5900	Ostomy pouch and accessories	I
876.5920	Protective garment for incontinence	I
876.5955	Peritoneo-venous shunt	III
876.5970	Hernia support	I
876.5980	Gastrointestinal tube and accessories	II

GENERAL HOSPITAL AND PERSONAL USE DEVICES

FR October 21, 1980

Monitoring Devices

Section	Device	Class
880.2200	Liquid crystal forehead temperature strip	II
880.2400	Bed-patient monitor	I
880.2420	Electronic monitor for gravity flow infusion systems	II
880.2440	Neonatal ventilatory effort monitor (apnea detector)	II
880.2460	Electrically powered spinal fluid pressure monitor	II
880.2500	Spinal fluid manometer	II
880.2700	Stand-on patient scale	I
880.2720	Patient scale	I. II
880.2740	Surgical sponge scale	I
880.2800	Sterilization process indicator	II
880.2900	Clinical color change thermometer	II
880.2910	Clinical electronic thermometer	II
880.2920	Clinical mercury thermometer	II

Therapeutic Devices

Section	Device	Class
880.5025	I.V. container	II
880.5045	Medical recirculating air cleaner	II
880.5075	Elastic bandage	I
880.5090	Liquid bandage	I
880.5100	AC-powered adjustable hospital bed	II
880.5110	Hydraulic adjustable hospital bed	I
880.5120	Manual adjustable hospital bed	I
880.5130	Infant radiant warmer	III
880.5140	Pediatric hospital bed	II
880.5150	Nonpowered flotation therapy mattress	I
880.5160	Therapeutic medical binder	I
880.5180	Burn sheet	I
880.5200	Intravascular catheter	II
880.5210	Intravascular catheter securement device	I
880.5240	Medical adhesive tape and adhesive bandage	I
880.5270	Neonatal eye pad	I
880.5300	Medical absorbent fiber	I
880.5400	Neonatal incubator	II
880.5410	Neonatal transport incubator	II
880.5420	Pressure infusor for an I.V. bag	I
880.5430	Nonelectrically powered fluid injector	II
880.5440	Intravascular administration set	II
880.5450	Patient care reverse isolation chamber	II
880.5475	Jet lavage	II
880.5500	AC-powered patient lift	II
880.5510	Non-AC powered patient lift	I
880.5550	Alternating pressure air flotation mattress	II
880.5560	Temperature regulated water mattress	II
880.5570	Hypodermic single lumen needle	II
880.5630	Nipple shield	I
880.5640	Lamb feeding nipple	I
880.5680	Pediatric position holder	I
880.5700	Neonatal phototherapy unit	II
880.5725	Infusion pump	II
880.5740	Suction snakebite kit	I
880.5760	Chemical cold pack snakebite kit	III
880.5780	Medical support stocking	I, II
880.5820	Therapeutic scrotal support	I
880.5860	Piston syringe	II
880.5950	Umbilical occlusion device	I

Miscellaneous Devices

Section	Device	Class
880.6025	Absorbent tipped applicator	I
880.6050	Ice bag	I
880.6060	Medical disposable bedding	I
880.6070	Bed board	I
880.6080	Cardiopulmonary resuscitation board	I
880.6085	Hot/cold water bottle	I
880.6100	Ethylene oxide gas aerator cabinet	II
880.6140	Medical chair and table	I
880.6150	Ultrasonic cleaner for medical instruments	I
880.6175	Specimen container	I
880.6185	Cast cover	I
880.6190	Mattress cover for medical purposes	I
880.6200	Ring cutter	I
880.6230	Tongue depressor	I
880.6250	Patient examination glove	I
880.6265	Examination gown	I
880.6280	Medical insole	I
880.6320	AC-powered medical examination light	II
880.6350	Battery-powered medical examination light	I
880.6375	Patient lubricant	I
880.6430	Liquid medication dispenser	I
880.6450	Skin pressure protector	I
880.6500	Medical ultraviolet air purifier	II
880.6710	Medical ultraviolet water purifier	II
880.6730	Body waste receptacle	I
880.6740	Vacuum-powered body fluid suction apparatus	II
880.6760	Protective restraint	I
880.6775	Powered patient transfer device	II
880.6785	Manual patient transfer device	I
880.6800	Washer for body waste receptacles	I
880.6820	Medical disposable scissors	I
880.6850	Sterilization wrap	II
880.6860	Ethylene oxide gas sterilizer	II
880.6870	Dry-heat sterilizer	II
880.6880	Steam sterilizer	II
880.6900	Hand-carried stretcher	I
880.6910	Wheeled stretcher	II
880.6920	Syringe needle introducer	II
880.6960	Irrigating syringe	I
880.6970	Liquid crystal vein location	I
880.6980	Vein stabilizer	I

GENERAL AND PLASTIC SURGERY

FR June 24, 1988

Diagnostic Devices

Section	Device	Class
878.1800	Speculum and accessories	I

Prosthetic Devices

Section	Device	Class
878.3250	External facial fracture fixation appliance	I
878.3300	Surgical mesh	II
878.3500	Polytetrafluoroethylene with carbon fibers composite implant material	II
878.3530	Silicone inflatable breast prosthesis	III
878.3540	Silicone gel-filled breast prosthesis	III
878.3550	Chin prosthesis	II
878.3590	Ear prosthesis	II
878.3610	Esophageal prosthesis	III
878.3680	Nose prosthesis	II
878.3720	Tracheal prosthesis	III
878.3750	External prosthesis adhesive	I
878.3800	External aesthetic restoration prosthesis	I
878.3900	Inflatable extremity splint	I
878.3910	Noninflatable extremity splint	I
878.3925	Plastic surgery kit and accessories	I

Surgical Devices

Section	Device	Class
878.4040	Surgical apparel	I, II
878.4100	Organ bag	I
878.4160	Surgical camera and accessories	I
878.4200	Introduction/drainage catheter and accessories	I
878.4300	Implantable clip	II
878.4320	Removable skin clip	I
878.4350	Cryosurgical unit and accessories	II
878.4370	Surgical drape and drape accessories	II
878.4380	Drape adhesive	I
878.4400	Electrosurgical cutting and coagulation device and accessories	II

878.4460	Surgeon's glove	I
878.4470	Surgeon's gloving cream	I
878.4480	Absorbable powder for lubricating a surgeon's glove	III
878.4490	Absorbable hemostatic agent and dressing	III
878.4520	Polytetrafluoroethylene injectable	III
878.4580	Surgical lamp	II
878.4630	Ultraviolet lamp for dermatologic disorders	II
878.4635	Ultraviolet lamp for tanning	
878.4660	Skin marker	I
878.4680	Nonpowered, single patient, portable suction apparatus	I
878.4700	Surgical microscope and accessories	
878.4730	Surgical skin degreaser or adhesive tape solvent	I
878.4750	Implantable staple	II
878.4760	Removable skin staple	I
878.4780	Powered suction pump	II
878.4800	Manual surgical instrument for general use	I
878.4810	Laser surgical instrument for use in general and plastic surgery and in dermatology	II
878.4820	AC-powered, battery-powered and pneumatically powered surgery instrument motors and accessories attachments	
878.4930	Suture retention device	I
878.4950	Manual operating table and accessories and manual operating chair and accessories	I
878.4960	Air or AC-powered operating table and accessories and air or AC-powered operating chair and accessories	

Therapeutic Devices

Section	Device	Class
878.5070	Air-handling apparatus for a surgical operating room	II
878.5350	Needle-type epilator	II
878.5360	Tweezer-type epilator	III
878.5650	Topical oxygen chamber for extremities	III
878.5900	Nonpneumatic tourniquet	I
878.5910	Pneumatic tourniquet	II

HEMATOLOGY AND PATHOLOGY

FR September 12, 1980

Biological Stains

Section	Device	Class
864.1850	Dye and chemical solution stains	I

Cell and Tissue Culture Products

Section	Device	Class
864.2220	Synthetic cell and tissue culture media and components	I
864.2240	Cell and tissue culture supplies and equipment	I
864.2260	Chromosome culture kit	I
864.2280	Cultured animal and human cells	I
864.2360	Mycoplasma detection media and components	I
864.2800	Animal and human sera	I
864.2875	Balanced salt solutions or formulations	I

Pathology - Instrumentation and Accessories

Section	Device	Class
864.3010	Tissue processing equipment	I
864.3250	Specimen transport and storage container	I
864.3300	Cytocentrifuge	I
864.3400	Device for sealing microsections	I
864.3600	Microscopes and accessories	I
864.3800	Automated slide stainer	I
864.3875	Automated tissue processor	I

Specimen Preparation Reagents

Section	Device	Class
864.4010	General purpose reagent	I
864.4400	Enzyme preparations	I

Automated and Semiautomated Hematology Devices

Section	Device	Class
864.5200	Automated cell counter	II
864.5220	Automated differential cell counter	III
864.5240	Automated blood cell diluting apparatus	I
864.5260	Automated cell locating device	II
864.5300	Red cell indices device	II
864.5350	Microsedimentation centrifuge	I
864.5400	Coagulation instrument	II
864.5425	Multipurpose system for in vitro coagulation studies	II

864.5600	Automated hematocrit instrument	II
864.5620	Automated hemoglobin system	II
864.5680	Automated heparin analyzer	III
864.5700	Automated platelet aggregation system	II
864.5800	Automated sedimentation rate device	I
864.5850	Automated slide spinner	I
864.5950	Blood volume measuring device	II

Manual Hematology Devices

Section	Device	Class
864.6100	Bleeding time device	II
864.6150	Capillary blood collection tube	I
864.6160	Manual blood cell counting device	I
864.6400	Hematocrit measuring device	II
864.6550	Occult blood test	II
864.6600	Osmotic fragility test	I
864.6650	Platelet adhesion test	II
864.6675	Platelet aggregometer	II
864.6700	Erythrocyte sedimentation rate test	I

Hematology Kits and Packages

Section	Device	Class
864.7040	Adenosine triphosphate release assay	I
864.7060	Antithrombin III assay	II
864.7100	Red blood cell enzyme assay	II
864.7140	Activated whole blood clotting time test	II
864.7250	Erythropoietin assay	III
864.7275	Euglobulin lysis time test	II
864.7290	Factor deficiency test	II
864.7300	Fibrin monomer paracoagulation test	III
864.7320	Fibrinogen/fibrin degradation products assay	II
864.7340	Fibrinogen determination system	II
864.7360	Erythrocytic glucose-6 phosphate dehydrogenase assay	II
864.7375	Glutathione reductase assay	II
864.7400	Hemoglobin A2 assay	II
864.7415	Abnormal hemoglobin assay	II
864.7425	Carboxyhemoglobin assay	II
864.7440	Electrophoretic hemoglobin analysis system	II
864.7455	Fetal hemoglobin assay	II
864.7470	Glycosylated hemoglobin assay	II
864.7490	Sulfhemoglobin assay	II
864.7500	Whole blood hemoglobin assay	II
864.7525	Heparin assay	II
864.7660	Leukocyte alkaline phosphatase test	I

864.7675	Leukocyte peroxidase test	I
864.7695	Platelet factor 4 radioimmunoassay	II
864.7720	Prothrombin consumption test	II
864.7735	Prothrombin-proconvertin test and thrombotest	II
864.7750	Prothrombin time test	II
864.7825	Sickle cell test	II
864.7875	Thrombin time test	II
864.7900	Thromboplastin generation test	I
864.7925	Partial thromboplastin time test	II

Hematology Reagents

Section	Device	Class
864.8100	Bothrops atrox reagent	II
864.8150	Calibrator for cell indices	II
864.8165	Calibrator for hemoglobin or hematocrit measurement	II
864.8175	Calibrator for platelet counting	II
864.8185	Calibrator for red cell and white cell counting	II
864.8200	Blood cell diluent	I
864.8500	Lymphocyte separation medium	I
864.8540	Red cell lysing reagent	I
864.8625	Hematology quality control mixture	II
864.8950	Russell viper venom reagent	I

Products Used in Establishments That Manufacture Blood and Blood Products

Section	Device	Class
864.9050	Blood bank supplies	I
864.9100	Empty container for the collection and processing of blood and blood components	II
864.9125	Vacuum-assisted blood collection system	I
864.9145	Processing system for frozen blood	II
864.9160	Blood group substances of nonhuman origin for in vitro diagnostic use	II
864.9175	Automated blood grouping and antibody test system	II
864.9185	Blood grouping view box	I
864.9195	Blood mixing devices and blood weighing device	I
864.9205	Blood and plasma warming device	II, III
864.9225	Cell-freezing apparatus and reagents for in vitro diagnostic use	I
864.9245	Automated blood cell separator	III
864.9275	Blood bank centrifuge for in vitro diagnostic use	I
864.9285	Automated cell-washing centrifuge for immuno-hematology	II
864.9300	Automated Coombs test system	II
864.9320	Copper sulfate solution for specific gravity determinations	I
864.9400	Stabilized enzyme solution	II

864.9550	Lectins and protectins	II
864.9575	Environmental chamber for storage of platelet concentrate	II
364.9600	Potentiating media for in vitro diagnostic use	II
864.9650	Quality control kit for blood banking reagents	II
864.9700	Blood storage refrigerator and blood storage freezer	II
864.9750	Heat-sealing device	I
864.9875	Transfer set	I

IMMUNOLOGY AND MICROBIOLOGY

FR November 9, 1982

Diagnostic Devices

Section	Device	Class
866.1620	Antimicrobial susceptibility test disc	II
866.1640	Antimicrobial susceptibility test powder	II
866.1700	Culture medium for antimicrobial susceptibility tests	II

Microbiology Devices

Section	Device	Class
866.2050	Staphylococcal typing bacteriophage	I
866.2120	Anaerobic chamber	I
866.2160	Coagulase plasma	II
866.2170	Automated colony counter	I
866.2180	Manual colony counter	I
866.2300	Multipurpose culture medium	I
866.2320	Differential culture medium	I
866.2330	Enriched culture medium	I
866.2350	Microbiological assay culture medium	I
866.2360	Selective culture medium	I
866.2390	Transport culture medium	I
866.2410	Culture medium for pathogenic Neisseria spp.	II
866.2420	Oxidase screening test for gonorrhea	III
866.2440	Automated medium dispensing and stacking device	I
866.2450	Supplement for culture media	I
866.2480	Quality control kit for culture media	I
866.2500	Microtiter diluting and dispensing device	I
866.2540	Microbiological incubator	I
866.2560	Microbial growth monitor	I
866.2580	Gas-generating device	I
866.2600	Wood's fluorescent lamp	I

866.2660	Microorganism differentiation and identification device	I
866.2850	Automated zone reader	I
866.2900	Microbiological specimen collection and transport device	I

Serological Reagents

Section	Device	Class
866.3010	Acinetobacter calcoaceticus serological reagents	I
866.3020	Adenovirus serological reagents	I
866.3035	Arizona spp. serological reagents	I
866.3040	Aspergillus spp. serological reagents	I
866.3060	Blastomyces dermatitidis serological reagents	II
866.3065	Bordetella spp. serological reagents	I
866.3085	Brucella spp. serological reagents	II
866.3110	Campylobacter fetus serological reagents	I
866.3120	Chlamydia serological reagents	I
866.3125	Citrobacter spp. serological reagents	I
866.3135	Coccidioides immitis serological reagents	II
866.3140	Corynebacterium spp. serological reagents	I
866.3145	Coxsackievirus serological reagents	I
866.3165	Cryptococcus neoformans serological reagents	II
866.3175	Cytomegalovirus serological reagents	II
866.3200	Echinococcus spp. serological reagents	I
866.3205	Echovirus serological reagents	I
866.3220	Entamoeba histolytica serological reagents	II
866.3235	Epstein-Barr virus serological reagents	I
866.3240	Equine encephalomyelitis virus serological reagents	I
866.3250	Erysipelothrix rhusiopathiae serological reagents	I
866.3255	Escherichia coli serological reagents	I
866.3270	Flavobacterium spp. serological reagents	I
866.3280	Francisella tularensis serological reagents	II
866.3290	Gonococcal antibody test (GAT)	III
866.3300	Haemophilus spp. serological reagents	II
866.3305	Herpes simplex virus serological reagents	III
866.3320	Histoplasma capsulatum serological reagents	II
866.3330	Influenza virus serological reagents	I
866.3340	Klebsiella spp. serological reagents	I
866.3350	Leptospira spp. serological reagents	II
866.3355	Listeria spp. serological reagents	I
866.3360	Lymphocytic choriomeningitis virus serological reagents	I
866.3370	Mycobacterium tuberculosis immunofluorescent reagents	I
866.3375	Mycoplasma spp. serological reagents	I
866.3380	Mumps virus serological reagents	I
866.3390	Neisseria spp. direct serological test reagents	II
866.3400	Parainfluenza virus serological reagents	I
866.3405	Poliovirus serological reagents	I
866.3410	Proteus spp. (Weil-Felix) serological reagents	I
866.3415	Pseudomonas spp. serological reagents	II
866.3460	Rabiesvirus immunofluorescent reagents	II
866.3470	Reovirus serological reagents	I

866.3480	Respiratory syncytial virus serological reagents	I
866.3490	Rhinovirus serological reagents	I
866.3500	Rickettsia serological reagents	I
866.3510	Rubella virus serological reagents	III
866.3520	Rubeola (measles) virus serological reagents	I
866.3550	Salmonella spp. serological reagents	II
866.3600	Schistosoma spp. serological reagents	I
866.3630	Serratia spp. serological reagents	I
866.3660	Shigella spp. serological reagents	II
866.3680	Sporothrix schenckii serological reagents	I
866.3700	Staphylococcus aureus serological reagents	I
866.3720	Streptococcus spp. exoenzyme reagents	II
866.3740	Streptococcus spp. serological reagents	I
866.3780	Toxoplasma gondii serological reagents	II
866.3820	Treponema pallidum nontreponemal test reagents	II
866.3830	Treponema pallidum treponemal test reagents	II
866.3850	Trichinella spiralis serological reagents	I
866.3870	Trypanosoma spp. serological reagents	I
866.3900	Varicealla-zoster virus serological reagents	II
866.3930	Vibrio cholerae serological reagents	II

Immunology Laboratory Equipment and Reagents

Section	Device	Class
866.4100	Complement reagent	I
866.4500	Immunoelectrophoresis equipment	I
866.4520	Immunofluorometer equipment	I
866.4540	Immunonephelometer equipment	I
866.4600	Ouchteriony agar plate	I
866.4800	Radial immunodiffusion plate	I
866.4830	Rocket immunoelectrophoresis equipment	I
866.4900	Support gel	I

Immunological Test Systems

Section	Device	Class
866.5040	Albumin immunological test system	II
866.5060	Prealbumin immunological test system	I
866.5065	Human allotypic marker immunological test system	I
866.5080	Alpha-1 antichymotrypsin immunologial test system	II
866.5090	Antimitochondrial antibody immunological test system	II
866.5100	Antinuclear antibody immunological test system	II
866.5110	Antiparietal antibody immunological test system	II
866.5120	Antismooth muscle antibody immunological test system	II
866.5130	Alpha-1-antitrypsin immunological test system	II
866.5150	Bence-Jones proteins immunological test system	II

866.5160	Beta-globulin immunological test system	I
866.5170	Breast milk immunological test system	I
866.5200	Carbonic anydrase B and C immunological test system	I
866.5210	Ceruloplasmin immunological test system	II
866.5220	Cohn fraction II immunological test system	I
866.5230	Colostrum immunological test system	I
866.5240	Complement components immunological test system	II
866.5250	Complement C_1 inhibitor (inactivator) immunological test system	II
866.5260	Complement C_{3b} inactivator immunological test system	II
866.5270	C-reactive protein immunological test system	II
866.5320	Properdin factor B immunological test system	II
866.5330	Factor XIII, A, S, immunological test system	I
866.5340	Ferritin immunological test system	II
866.5350	Fibrinopeptide A immunological test system	II
866.5360	Cohn fraction IV immunological test system	I
866.5370	Cohn fraction V immunological test system	I
866.5380	Free secretory component immunological test system	II
866.5400	Alpha-globulin immunological test system	I
866.5420	Alpha-1-glycoproteins immunological test system	I
866.5425	Alpha-2-glycoproteins immunological test system	I
866.5430	Beta-2-glycoprotein I immunological test system	I
866.5440	Beta-2-glycoprotein III immunological test system	I
866.5460	Haptoglobin immunological test system	II
866.5470	Hemoglobin immunological test system	II
866.5490	Hemopexin immunological test system	II
866.5500	Hypersensitivity pneumonitis immunological test system	II
866.5510	Immunoglobulins A, G, M, D, and E immunological test system	II
866.5520	Immunoglobulin G (Fab fragment specific) immunological test system	II
866.5530	Immunoglobulin G (Fc fragment specific) immunological test system	II
866.5540	Immunoglobulin G (Fd fragment specific) immunological test system	I
866.5550	Immunoglobulin (light chain specific) immunological test system	II
866.5560	Lactic dehydrogenase immunological test system	I
866.5570	Lactoferrin immunological test system	I
866.5580	Alpha-1-lipoprotein immunological test system	II
866.5590	Lipoprotein X immunological test system	I
866.5600	Low-density lipoprotein immunological test system	II
866.5620	Alpha-2-macroglobulin immunological test system	II
866.5630	Beta-2-microglobulin immunological test system	II
866.5640	Infectious mononucleosis immunological test system	II
866.5660	Multiple autoantibodies immunological test system	II
866.5680	Myoglobin immunological test system	II
866.5700	Whole human plasma or serum immunological test system	I
866.5715	Plasminogen immunological test system	I
866.5735	Prothrombin immunological test system	I
866.5750	Radioallergosorbent (RAST) immunological test system	II
866.5765	Retinol-binding protein immunological test system	I
866.5775	Rheumatoid factor immunological test system	II
866.5800	Seminal fluid (sperm) immunological test system	I
866.5820	Systemic lupus erythematosus immunological test system	II

866.5860	Total spinal fluid immunological test system	II
866.5870	Thyroid autoantibody immunological test system	II
866.5880	Transferrin immunological test system	II
866.5890	Inter-alpha trypsin inhibitor immunological test system	I

Tumor Associated Antigen Immunological Test Systems

Section	Device	Class
866.6010	Carcinoembryonic antigen (CEA) immunological test system as an aid in the detection and management of cancer	III

NEUROLOGY

FR September 4, 1979

Diagnostic Devices

Section	Device	Class
882.1020	Rigidity analyzer	II
882.1030	Ataxiagraph	I
882.1200	Two-point discriminator	I
882.1240	Echoencephalograph	II
882.1275	Electroconductive media	II
882.1310	Cortical electrode	II
882.1320	Cutaneous electrode	II
882.1330	Depth electrode	II
882.1340	Nasopharyngeal electrode	II
882.1350	Needle electrode	II
882.1400	Electroencephalograph	II
882.1410	Electroencephalograph electrode/lead tester	II
882.1420	Electroencephalogram (EEG) signal spectrum analyzer	I
882.1430	Electroencephalograph test signal generator	I
882.1460	Nystagmograph	II
882.1480	Neurological endoscope	II
882.1500	Esthesiometer	I
882.1525	Tuning fork	I
882.1540	Galvanic skin response measurement device	II
882.1550	Nerve conduction velocity measurement device	II
882.1560	Skin potential measurement device	II
882.1570	Powered direct-contact temperature measurement device	II
882.1610	Alpha monitor	II
882.1620	Intracranial pressure monitoring device	II

882.1700	Percussor	I
882.1750	Pinwheel	I
882.1790	Ocular plethysmograph	III
882.1825	Rheoencephalograph	III
882.1835	Physiological signal amplifier	II
882.1845	Physiological signal conditioner	II
882.1855	Electroencephalogram (EEG) telemetry system	II
882.1870	Evoked response electrical stimulator	II
882.1880	Evoked response mechanical stimulator	II
882.1890	Evoked response photic stimulator	II
882.1900	Evoked response auditory stimulator	II
882.1925	Ultrasonic scanner calibration test block	I
882.1950	Tremor transducer	II

Surgical Devices

Section	Device	Class
882.4030	Skull plate anvil	I
882.4060	Ventricular cannula	I
882.4100	Ventricular catheter	II
882.4125	Neurosurgical chair	I
882.4150	Scalp clip	II
882.4175	Aneurysm clip applier	II
882.4190	Clip forming/cutting instrument	I
882.4200	Clip removal instrument	I
882.4215	Clip rack	I
882.4250	Cryogenic surgical device	II
882.4275	Dowel cutting instrument	II
882.4300	Manual cranial drill, burr, trephine, and accessories	II
882.4305	Powered compound cranial drill, burr, trephine, and accessories	II
882.4310	Powered simple cranial drill, burr, trephine, and accessories	II
882.4325	Cranial drill handpiece (brace)	II
882.4360	Electric cranial drill motor	II
882.4370	Pneumatic cranial drill motor	II
882.4400	Radiofrequency lesion generator	II
882.4440	Neurosurgical headrest	I
882.4460	Neurosurgical head holder (skull clamp)	II
882.4500	Cranioplasty material forming instrument	I
882.4525	Microsurgical instrument	I
882.4535	Nonpowered neurosurgical instrument	I
882.4545	Shunt system implantation instrument	I
882.4560	Stereotaxic instrument	II
882.4600	Leukotome	I
882.4650	Neurosurgical suture needle	I
882.4700	Cottonoid paddie	II
882.4725	Radiofrequency lesion probe	II
882.4750	Skull punch	I
882.4800	Self-retaining retractor for neurosurgery	II

882.4840	Manual rongeur	II
882.4845	Powered rongeur	II
882.4900	Skullplate screwdriver	I

Therapeutic Devices

Section	Device	Class
882.5030	Methyl methacrylate for aneurysmorrhaphy	II
882.5050	Biofeedback device	II
882.5070	Bite block	II
882.5150	Intravascular occluding catheter	III
882.5175	Carotid artery clamp	II
882.5200	Aneurysm clip	II
882.5225	Implanted malleable clip	II
882.5235	Aversive conditioning device	II
882.5250	Burr hole cover	II
882.5275	Nerve cuff	II
882.5300	Methyl methacrylate for cranioplasty	II
882.5320	Preformed alterable cranioplasty plate	II
882.5330	Preformed nonalterable cranioplasty plate	II
882.5360	Cranioplasty plate fastener	II
882.5500	Lesion temperature monitor	II
882.5550	Central nervous system fluid shunt and components	II
882.5800	Cranial electrotherapy stimulator	III
882.5810	External functional neuromuscular stimulator	II
882.5820	Implanted cerebellar stimulator	III
882.5830	Implanted diaphragmatic/phrenic nerve stimulator	III
882.5840	Implanted intracerebral/subcortical stimulator for pain relief	III
882.5850	Implanted spinal cord stimulator for bladder evacuation	III
882.5860	Implanted neuromuscular stimulator	III
882.5870	Implanted peripheral nerve stimulator for pain relief	II
882.5880	Implanted spinal cord stimulator for pain relief	II
882.5890	Transcutaneous electrical nerve stimulator for pain relief	II
882.5900	Preformed craniosynostosis strip	II
882.5910	Dura substitute	II
882.5940	Electroconvulsive therapy device	III
882.5950	Artificial embolization device	III
882.5960	Skull tong for traction	II

OBSTETRICAL AND GYNECOLOGICAL

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Diagnostic Devices

Section	Device	Class
884.1040	Viscometer for cervical mucus	I
884.1050	Endocervical aspirator	II
884.1060	Endometrial aspirator	III
884.1100	Endometrial brush	III
884.1175	Endometrial suction curette and accessories	II
884.1185	Endometrial washer	III
884.1300	Uterotubal carbon dioxide insufflator and accessories	II
884.1425	Perineometer	II
884.1550	Amniotic fluid sampler (amniocentesis tray)	II
884.1560	Fetal blood sampler	II
884.1600	Transabdominal amnioscope (fetoscope) and accessories	III
884.1630	Colposcope	II
884.1640	Culdoscope and accessories	II
884.1660	Transcervical endoscope (amnioscope) and accessories	II
884.1690	Hysteroscope and accessories	II
884.1700	Hysteroscopic insufflator	II
884.1720	Gynecologic laparoscope and accessories	II
884.1730	Laparoscopic insufflator	II

Monitoring Devices

Section	Device	Class
884.2050	Obstetric data analyzer	III
884.2225	Obstetric-gynecologic ultrasonic imager	II
884.2600	Fetal cardiac monitor	II
884.2620	Fetal electroencephalographic monitor	III
884.2640	Fetal phonocardiographic monitor and accessories	II
884.2660	Fetal ultrasonic monitor and accessories	II
884.2675	Fetal scalp circular (spiral) electrode and applicator	II
884.2685	Fetal scalp clip electrode and applicator	III
884.2700	Intrauterine pressure monitor and accessories	II
884.2720	External uterine contraction monitor and accessories	II
884.2740	Perinatal monitoring system and accessories	II
884.2900	Fetal stethoscope	I
884.2960	Obstetric ultrasonic transducer and accessories	II

Prosthetic Devices

Section	Device	Class
884.3200	Cervical drain	II
884.3575	Vaginal pessary	II
884.3650	Fallopian tube prosthesis	II
884.3900	Vaginal stent	II

Gynecological Surgical Devices

Section	Device	Class
884.4100	Endoscopic electrocautery and accessories	III
884.4120	Gynecologic electrocautery and accessories	II
884.4150	Bipolar endoscopic coagulator-cutter and accessories	III
884.4160	Unipolar endoscopic coagulator-cutter and accessories	II
884.4250	Expandable cervical dilator	III
884.4260	Hygroscopic Laminaria cervical dilator	II
884.4270	Vibratory cervical dilator	III
884.4340	Fetal vacuum extractor	II
884.4400	Obstetric forceps	II
884.4500	Obstetric fetal destructive instrument	II
884.4520	Obstetric-gynecologic general manual instrument	I
884.4530	Obstetric-gynecologic specialized manual instrument	II
884.4550	Gynecologic surgical laser	II
884.4900	Obstetric table and accessories	II

Therapeutic Devices

Section	Device	Class
884.5050	Metreurynter-balloon abortion system	III
884.5070	Vacuum abortion system	II
884.5100	Obstetric anesthesia set	II
884.5150	Nonpowered breast pump	I
884.5160	Powered breast pump	II
884.5225	Abdominal decompression chamber	III
884.5250	Cervical cap	II
884.5300	Condom	II
884.5350	Contraceptive diaphragm and accessories	II
884.5360	Contraceptive intrauterine device (IUD) and introducer	III
884.5380	Contraceptive tubal occlusion device (TOD) and introducer	III
884.5390	Perineal heater	II
884.5400	Menstrual cup	II
884.5425	Scented menstrual pad	II

884.5435	Unscented menstrual pad	I
884.5460	Scented menstrual tampon	II
884.5470	Unscented menstrual tampon	II
884.5900	Therapeutic vaginal douche apparatus	II
884.5920	Vaginal insufflator	I
884.5940	Powered vaginal muscle stimulator for therapeutic use	III
884.5960	Genital vibrator for therapeutic use	II

OPHTHALMIC DEVICES

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Diagnostic Devices

Section	Device	Class
886.1040	Ocular esthesiometer	I
886.1050	Adaptometer (biophotometer)	
886.1070	Anomaloscope	
886.1090	Haidinger brush	
886.1120	AC-powered ophthalmic camera	
886.1140	Ophthalmic chair	I
886.1140	Ophthalmic chair (AC-powered)	
886.1150	Visual acuity chart*	I
886.1160	Color vision plate illuminator	
886.1170	Color vision tester	I
886.1190	Distometer	I
886.1200	Optokinetic drum	I
886.1220	Corneal electrode	II
886.1250	Euthyscope	I
886.1250	Euthyscope (AC-powered)	
886.1270	Exophthalmometer	I
886.1290	AC-powered fixation device	
886.1300	Afterimage flasher	
886.1320	Fornixscope	I
886.1330	Amsler grid	I
886.1340	Haploscope	
886.1350	Keratoscope	I
886.1350	Keratoscope (AC-powered)	
886.1360	Visual field laser instrument	II
886.1375	Bagolini lens	I
886.1380	Diagnostic condensing lens	I
886.1385	Polymethylmethacrylate (PMMA) diagnostic contact lens	II
886.1390	Flexible diagnostic Fresnel lens	I
886.1395	Diagnostic Hruby fundus lens	I
886.1400	Maddox lens	I
886.1405	Ophthalmic trial lens set	II
886.1410	Ophthalmic trial lens clip	I
886.1415	Ophthalmic trial lens frame	I

886.1420	Ophthalmic lens gauge	I
886.1425	AC-powered lens measuring instrument	
886.1430	Ophthalmic contact lens radius measuring device	
886.1435	AC-powered Maxwell spot	
886.1450	Corneal radius measuring device	
886.1460	Stereopsis measuring instrument	I
886.1500	Headband mirror	I
886.1510	Eye movement monitor	II
886.1570	Ophthalmoscope*	II
886.1605	Perimeter	I
886.1605	Perimeter (AC-powered)	
886.1630	AC-powered photostimulator	II
886.1640	Ophthalmic preamplifier	II
886.1650	Ophthalmic bar prism	I
886.1655	Ophthalmic Fresnel prism	I
886.1660	Gonioscopic prism	I
886.1665	Ophthalmic rotary prism	I
886.1670	Ophthalmic isotope uptake probe	II
886.1680	Ophthalmic projector	
886.1690	Pupillograph	
886.1700	Pupillometer	I
886.1700	Pupillometer (AC-powered)	
886.1750	Skiascopic rack	II
886.1760	Ophthalmic refractometer	II
886.1770	Manual refractor	I
886.1780	Retinoscope	I
886.1780	Retinoscope (AC-powered)	
886.1790	Nearpoint ruler	I
886.1800	Schirmer strip	I
886.1810	Tangent screen (campimeter)	I
886.1810	Tangent screen (campimeter) (AC-powered)	
886.1840	Simulatan (including crossed cylinder)	I
886.1850	AC-powered slitlamp biomicroscope	II
886.1860	Ophthalmic instrument stand	I
886.1860	Ophthalmic instrument stand (AC-powered)	
886.1870	Stereoscope	I
886.1870	Stereoscope (AC-powered)	
886.1880	Fusion and stereoscopic target	I
886.1905	Nystagmus tape	I
886.1910	Spectacle dissociation test system	I
886.1910	Spectacle dissociation test system (AC-powered)	
886.1930	Tonometer and accessories	II
886.1940	Tonometer sterilizer	
886.1945	Transilluminator	I
886.1945	Transilluminator (AC-powered)	

Prosthetic Devices

Section	Device	Class
886.3100	Ophthalmic tantalum clip	II
886.3130	Ophthalmic conformer	II
886.3200	Artificial eye	II
886.3300	Absorbable implant (scleral buckling method)	II
886.3320	Eye sphere implant	II
886.3340	Extraocular orbital implant	II
886.3400	Keratoprosthesis	III
886.3600	Intraocular lens	III
886.3800	Scleral shell	II
886.3920	Eye valve implant	III

Surgical Devices

Section	Device	Class
886.4070	Powered corneal burr	I
886.4070	Powered corneal burr (AC-powered)	
886.4100	Radiofrequency electrosurgical cautery apparatus	II
886.4115	Thermal cautery unit	II
886.4150	Vitreous aspiration and cutting instrument*	II
886.4170	Cryophthalmic unit	II
886.4230	Ophthalmic knife test drum	I
886.4250	Ophthalmic electrolysis unit	I
886.4250	Ophthalmic electrolysis unit (AC-powered)	
886.4270	Intraocular gas	III
886.4275	Intraocular fluid	III
886.4280	Intraocular pressure measuring device	III
886.4300	Intraocular lens guide	I
886.4335	Operating headlamp	I
886.4335	Operating headlamp (AC-powered)	
886.4350	Manual ophthalmic surgical instrument	I
886.4360	Ocular surgery irrigation device	I
886.4370	Keratome	I
886.4370	Keratome (AC-powered)	
886.4390	Ophthalmic laser	II
886.4400	Electronic metal locator	II
886.4440	AC-powered magnet	II
886.4445	Permanent magnet	I
886.4570	Ophthalmic surgical marker	I
886.4610	Ocular pressure applicator	II
886.4650	Eye pad	
886.4670	Phacofragmentation system*	II
886.4690	Ophthalmic photocoagulator	II
886.4750	Ophthalmic eye shield	I

886.4770	Ophthalmic operating spectacles (loupes)	I
886.4790	Ophthalmic sponge	II
886.4855	Ophthalmic instrument table	I
886.4855	Ophthalmic instrument table (AC-powered)	

Therapeutic Devices

Section	Device	Class
886.5100	Ophthalmic beta radiation source	II
886.5120	Low-power binocular loupe	I
886.5400	Polymethylmethacrylate (PMMA) contact lens	
886.5420	Contact lens inserter/remover	I
886.5540	Low-vision magnifier	I
886.5600	Ptosis crutch	I
886.5800	Ophthalmic bar reader	I
886.5810	Ophthalmic prism reader	I
886.5820	Closed-circuit television reading system	
886.5840	Magnifying spectacles*	I
886.5842	Spectacle frame* (proposed as 886.5270)	I
886.5844	Prescription spectacle lens* (proposed as 886.5450)	I
886.5850	Sunglasses (nonprescription)*	II
886.5870	Low-vision telescope	I
886.5900	Electronic vision aid	I
886.5900	Electronic vision aid (AC-powered)	
886.5910	Image intensification vision aid	I
886.5915	Optical vision aid	I
886.5915	Optical vision aid (AC-powered)	
886.5916	Rigid gas permeable contact lens	III
886.5918	Rigid gas permeable contact lens solution	III
886.5925	Soft (hydrophilic) contact lens	III
886.5928	Soft (hydrophilic) contact lens solution	III
886.5933	Contact lens heat disinfection unit	III

ORTHOPEDIC DEVICES

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Diagnostic Devices

Section	Device	Class
888.1100	Arthroscope	II
888.1240	AC-powered dynamometer	II
888.1250	Nonpowered dynamometer	I
888.1500	AC-powered goniometer	
888.1520	Nonpowered goniometer	I

Prosthetic Devices

Section	Device	Class
888.3000	Bone cap	II
888.3010	Bone fixation cerclage	II
888.3015	Bone heterograft	
888.3020	Intramedullary fixation rod	II
888.3025	Passive tendon prosthesis	II
888.3027	Polymethylmethacrylate (PMMA) bone cement	III
888.3030	Single/multiple component metallic bone fixation appliances and accessories	II
888.3040	Smooth or threaded metallic bone fixation fastener	II
888.3050	Spinal interlaminal fixation orthosis	II
888.3060	Spinal intervertebral body fixation orthosis	II
888.3100	Ankle joint metal/composite semi-constrained cemented prosthesis	II
888.3110	Ankle joint metal/polymer semi-constrained cemented prosthesis	II
888.3120	Ankle joint metal/polymer non-constrained cemented prosthesis	III
888.3150	Elbow joint metal/metal or metal/polymer constrained uncemented prosthesis	III
888.3160	Elbow joint metal/polymer semi-constrained cemented prosthesis	II
888.3170	Elbow joint radial (hemi-elbow) polymer prosthesis	II
888.3180	Elbow joint humeral (hemi-elbow) metallic uncemented prosthesis	III
888.3200	Finger joint metal/metal constrained uncemented prosthesis	III
888.3210	Finger joint metal/metal constrained cemented prosthesis	III
888.3220	Finger joint metal/polymer constrained cemented prosthesis	III
888.3230	Finger joint polymer constrained prosthesis	II
888.3300	Hip joint metal constrained cemented or uncemented prosthesis	III

888.3310	Hip joint metal/polymer constrained cemented or uncemented prosthesis	III
888.3320	Hip joint metal/metal semi-constrained, with a cemented acetabular component, prosthesis	III
888.3330	Hip joint metal/metal semi-constrained, with an uncemented acetabular component, prosthesis	III
888.3340	Hip joint metal/composite semi-constrained cemented prosthesis	II
888.3350	Hip joint metal/polymer semi-constrained cemented prosthesis	II
888.3360	Hip joint femoral (hemi-hip) metallic cemented or uncemented prosthesis	II
888.3370	Hip joint (hemi-hip) acetabular metal cemented prosthesis	III
888.3380	Hip joint femoral (hemi-hip) trunnion-bearing metal/polyacetal cemented prosthesis	III
888.3390	Hip joint femoral (hemi-hip) metal/polymer cemented or uncemented prosthesis	II
888.3400	Hip joint femoral (hemi-hip) metallic resurfacing prosthesis	II
888.3410	Hip joint metal/polymer semi-constrained resurfacing cemented prosthesis	III
888.3480	Knee joint femorotibial metallic constrained cemented prosthesis	III
888.3490	Knee joint femorotibial metal/composite non-constrained cemented prosthesis	II
888.3500	Knee joint femorotibial metal/composite semi-constrained cemented prosthesis	II
888.3510	Knee joint femorotibial metal/polymer constrained cemented prosthesis	II
888.3520	Knee joint femorotibial metal/polymer non-constrained cemented prosthesis	II
888.3530	Knee joint femorotibial metal/polymer semi-constrained cemented prosthesis	II
888.3540	Knee joint patellofemoral polymer/metal semi-constrained cemented prosthesis	III
888.3550	Knee joint patellofemorotibial polymer/metal/metal constrained cemented prosthesis	III
888.3560	Knee joint patellofemorotibial polymer/metal/polymer semi-constrained cemented prosthesis	II
888.3570	Knee joint femoral (hemi-knee) metallic uncemented prosthesis	III
888.3580	Knee joint patellar (hemi-knee) metallic resurfacing uncemented prosthesis	II, III
888.3590	Knee joint tibial (hemi-knee) metallic resurfacing uncemented prosthesis	II
888.3640	Shoulder joint metal/metal or metal/polymer constrained cemented prosthesis	III
888.3650	Shoulder joint metal/polymer non-constrained cemented prosthesis	III
888.3660	Shoulder joint metal/polymer semi-constrained cemented prosthesis	III
888.3680	Shoulder joint glenoid (hemi-shoulder) metallic cemented prosthesis	III
888.3690	Shoulder joint humeral (hemi-shoulder) metallic uncemented prosthesis	II
888.3720	Toe joint polymer constrained prosthesis	II
888.3730	Toe joint phalangeal (hemi-toe) polymer prosthesis	II

888.3750	Wrist joint carpal lunate polymer prosthesis	II
888.3760	Wrist joint carpal scaphoid polymer prosthesis	II
888.3770	Wrist joint carpal trapezium polymer prosthesis	II
888.3780	Wrist joint polymer constrained prosthesis	II
888.3790	Wrist joint metal constrained cemented prosthesis	III
888.3800	Wrist joint metal/polymer semi-constrained cemented prosthesis	II
888.3810	Wrist joint ulnar (hemi-wrist) polymer prosthesis	II

Surgical Devices

Section	Device	Class
888.4150	Calipers for clinical use	I
888.4200	Cement dispenser	I
888.4210	Cement mixer for clinical use	I
888.4220	Cement monomer vapor evacuator	I
888.4230	Cement ventilation tube	I
888.4300	Depth gauge for clinical use	I
888.4540	Orthopedic manual surgical instrument	I
888.4580	Sonic surgical instrument and accessories/attachments	II
888.4600	Protractor for clinical use	I
888.4800	Template for clinical use	I
888.5850	Nonpowered orthopedic traction apparatus and accessories	I
888.5890	Noninvasive traction component	I
888.5940	Cast component	I
888.5960	AC-powered cast removal instrument	
888.5980	Manual cast application and removal instrument	I

PHYSICAL MEDICINE DEVICES

FR November 23, 1983

Physical Medicine Diagnostic Devices

Section	Device	Class
890.1175	Electrode cable	I
890.1225	Chronaximeter	II
890.1375	Diagnostic electromyograph	II
890.1385	Diagnostic electromyograph needle electrode	II
890.1450	Powered reflex hammer	II
890.1575	Force-measured platform	II

890.1600	Intermittent pressure measurement system	II
890.1615	Miniature pressure transducer	II
890.1850	Diagnostic muscle stimulator	II
890.1925	Isokinetic testing and evaluation system	II

Physical Medicine Prosthetic Devices

Section	Device	Class
890.3025	Prosthetic and orthotic accessory	I
890.3075	Cane	I
890.3100	Mechanical chair	I
890.3110	Electric positioning chair	II
890.3150	Crutch	I
890.3175	Flotation cushion	I
890.3410	External limb orthotic component	I
890.3420	External limb prosthetic component	I
890.3450	Mechanical automobile hand and foot driving control	II
890.3475	Limb orthosis	I
890.3490	Truncal orthosis	I
890.3500	External assembled lower limb prosthesis	II
890.3520	Plinth	I
890.3610	Rigid pneumatic structure orthosis	III
890.3640	Arm sling	I
890.3665	Congential hip dislocation abduction splint	I
890.3675	Denis Brown splint	I
890.3690	Powered wheeled stretcher	II
890.3700	Nonpowered communication system	I
890.3710	Powered communication system	II
890.3725	Powered environmental control system	II
890.3750	Mechanical table	I
890.3760	Powered table	II
890.3790	Cane. crutch. and walker tips and pads	I
890.3800	Motorized three-wheeled vehicle	II
890.3825	Mechanical walker	I
890.3850	Mechanical wheelchair	I
890.3860	Powered wheelchair	II
890.3880	Special grade wheelchair	II
890.3890	Stair-climbing wheelchair	III
890.3900	Standup wheelchair	II
890.3910	Wheelchair accessory	I
890.3920	Wheelchair component	I
890.3930	Wheelchair elevator	II
890.3940	Wheelchair platform scale	I

Physical Medicine Therapeutic Devices

Section	Device	Class
890.5050	Daily activity assist device	I
890.5100	Immersion hydrobath	II
890.5110	Paraffin bath	II
890.5125	Nonpowered sitz bath	I
890.5150	Powered patient transport	II
890.5160	Air-fluidized bed	II
890.5170	Powered flotation therapy bed	II
890.5180	Manual patient rotation bed	I
890.5225	Powered patient rotation bed	II
890.5250	Moist steam cabinet	II
890.5275	Microwave diathermy	II. III
890.5290	Shortwave diathermy	II. III
890.5300	Ultrasonic diathermy	II. III
890.5350	Exercise component	I
890.5360	Measuring exercise equipment	II
890.5370	Nonmeasuring exercise equipment	I
890.5380	Powered exercise equipment	II
890.5410	Powered finger exerciser	II
890.5500	Infrared lamp	II
890.5525	Iontophoresis device	II. III
890.5575	Powered external limb overload warning device	II
890.5650	Powered inflatable tube massager	II
890.5660	Therapeutic massager	II
890.5700	Cold pack	I
890.5710	Hot or cold disposable pack	I
890.5720	Water circulating hot or cold pack	II
890.5730	Moist heat pack	I
890.5740	Powered heating pad	II
890.5765	Pressure-applying device	I
890.5850	Powered muscle stimulator	II
890.5860	Ultrasound and muscle stimulator	II. III
890.5880	Multi-function physical therapy table	II
890.5900	Powered traction equipment	II
890.5925	Traction accessory	I
890.5940	Chilling unit	II
890.5950	Powered heating unit	II
890.5975	Therapeutic vibrator	II

RADIOLOGY DEVICES

FR January 20, 1988

Diagnostic Devices

Section	Device	Class
892.1100	Scintillation (gamma) camera	
892.1110	Positron camera	
892.1130	Nuclear whole body counter	
892.1170	Bone densitometer	II
892.1200	Emission computed tomography system	II
892.1220	Fluorescent scanner	II
892.1300	Nuclear rectilinear scanner	
892.1310	Nuclear tomography system	II
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892.1360	Radionuclide dose calibrator	II
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892.1710	Mammographic X-ray system	II
892.1720	Mobile X-ray system	II
892.1730	Photofluorographic X-ray system	II
892.1740	Tomographic X-ray system	II
892.1750	Computed tomography X-ray system	II

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892.1820	Pneumoencephalographic chair	II
892.1830	Radiologic patient cradle	II
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892.1870	Radiographic film/cassette changer programmer	II
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892.1950	Radiographic anthropomorphic phantom	I
892.1960	Radiographic intensifying screen	I
892.1970	Radiographic ECG/respirator synchronizer	
892.1980	Radiologic table	II

Therapeutic Devices

Section	Device	Class
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892.5300	Medical neutron radiation therapy system	II
892.5650	Manual radionuclide applicator system	I
892.5700	Remote controlled radionuclide applicator system	II
892.5710	Radiation therapy beamshaping block	II
892.5730	Radionuclide brachytherapy source	II
892.5740	Radionuclide teletherapy source*	I
892.5750	Radionuclide radiation therapy system	II
892.5770	Powered radiation therapy patient support assembly	II
892.5780	Light beam patient position indicator	II
892.5840	Radiation therapy simulation system	II
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3 ESTABLISHMENT REGISTRATION

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INTRODUCTION

Section 510 of the Federal Food, Drug, and Cosmetic Act (the Act) requires that domestic establishments engaged in the manufacture, preparation, propagation, compounding, assembly, or processing of medical devices intended for human use and commercial distribution (marketing) register their establishment with the Food and Drug Administration (FDA) on Form FDA 2891. Foreign manufacturers commercially distributing devices in the U.S. are not required to register. However, they are requested to do so.

WHO MUST REGISTER

Those who must register include:

- o manufacturers and other specified processors of devices;
- o manufacturers of device accessories which are sold to end users;
- o initiators or developers of device specifications;
- o repackagers and relabelers;
- o initial distributors (importers) of imported devices;
- o contract manufacturers; and
- o contract sterilizers.

Those not required to register include:

- o manufacturers of raw materials or components used in manufacturing a finished device;
- o manufacturers of general purpose articles such as mass spectrometers, etc.;
- o licensed practitioners (physicians, dentists, optometrists, etc.) who manufacture or alter devices solely for use in their practice;
- o pharmacies and other retail outlets that dispense or sell devices in the normal course of business;
- o persons who manufacture devices solely for use in research, teaching, or analysis and do not distribute them commercially;

- warehousers and wholesalers who do not alter or modify devices or their containers;
- carriers who receive, carry, hold, or deliver devices in their normal conduct of business;
- manufacturers or processors of veterinary devices; or
- persons whose primary responsibility to the users is to dispense a previously manufactured device or provide services or benefits through the use of such a device (e.g., hearing aid dispenser, optician, clinical laboratory, X-ray assembler, dental laboratory, orthotic or prosthetic retailer).

HOW TO REGISTER

To register an establishment, Form FDA 2891, "Initial Registration of Medical Device Establishment," is used. An essential aid is the "Medical Device Establishment Registration Information and Instructions" booklet included in this chapter. It contains information on the registration process, definitions, and specific instructions for completion of FDA 2891 as well as a sample form.

When registering, manufacturers should bear in mind these points:

- Do not use post office (P.O.) box numbers as addresses on the FDA 2891. FDA will not accept P.O. box numbers. The actual street address must be used unless the only street address is a rural route box number.
- The owner/operator is the corporation, subsidiary, affiliated company, partnership, or proprietor directly responsible for the activities of the registering establishment. In the case of small businesses, the name of the owner/operator usually is the same as the name of the registering establishment.
- The official correspondent is an important person for purposes of registration and listing. This is the person designated by the owner/operator to be responsible for:
    - the annual registration of the establishment;
    - contact with FDA for listing;
    - maintenance and submission of a current list of officers and directors to FDA upon request; and
    - the receipt of pertinent correspondence from FDA directed to and involving the owner/operator and/or any of the firm's establishments.

WHEN TO REGISTER

Establishments that are required to register must do so within 30 days of beginning an activity requiring registration.

WHERE TO SUBMIT

All copies of Form FDA 2891 are to be submitted to the following address (you may wish to make a photocopy for your own records):

Device Registration and Listing Branch (HFZ-342)
Center for Devices and Radiological Health
Food and Drug Administration
5600 Fishers Lane
Rockville, Maryland 20857

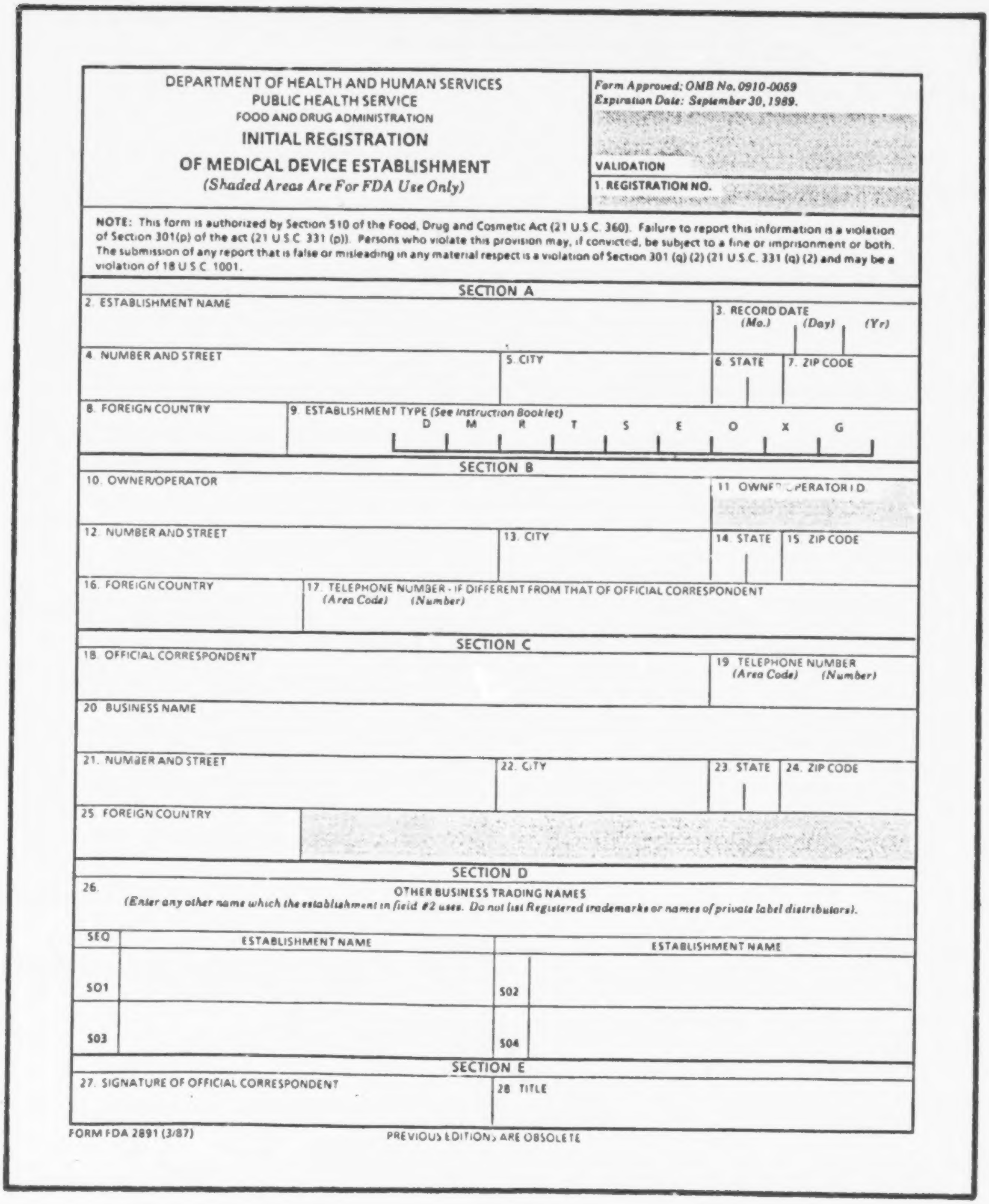
Within three to six weeks of receipt, the Device Registration and Listing Branch (DRLB) will return to the establishment a validated copy of its Form FDA 2891. This will include the establishment's registration and owner/operator identification (ID) numbers. In addition, the validated registration form will be accompanied by medical device listing materials for registered establishments required to list. For establishments required to both register and list, the Form FDA 2892 used for listing cannot be properly completed without the establishment's registration and owner/operator ID numbers which are included on the validated registration form.

UPDATING REGISTRATION DATA

Manufacturers must complete Form FDA 2891 for initial registration and Form FDA 2891(a) for all subsequent annual registrations. FDA forwards FDA 2891(a) forms to all establishments having valid device registrations for that year. The manufacturer must complete the form, including any necessary changes, and mail it to FDA by December 31. The top portion of Form FDA 2891(a) is separated and retained by the registrant as proof of annual registration.

Certain changes require notification by letter to the Device Registration and Listing Branch within 30 days of their occurrence. Any changes in individual ownership, corporate or partnership structure, official correspondent, or location of the registered device handling activity are to be submitted by letter to the Device Registration and Listing Branch. The letter should include the current registration number and a statement indicating that the information reflects a change from a previous submission. A record of any change in the names of officers and directors of a corporation must be maintained by the establishment's official correspondent, and shall be provided to the FDA upon receipt of a written request for the information.

INITIAL REGISTRATION OF MEDICAL DEVICE ESTABLISHMENT
(FDA 2891)



DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION
INITIAL REGISTRATION
OF MEDICAL DEVICE ESTABLISHMENT
(Shaded Areas Are For FDA Use Only)

Form Approved; OMB No. 0910-0059
Expiration Date: September 30, 1989.

VALIDATION

1. REGISTRATION NO.

NOTE: This form is authorized by Section 510 of the Food, Drug and Cosmetic Act (21 U.S.C. 360). Failure to report this information is a violation of Section 301(p) of the act (21 U.S.C. 331 (p)). Persons who violate this provision may, if convicted, be subject to a fine or imprisonment or both. The submission of any report that is false or misleading in any material respect is a violation of Section 301 (q) (2) (21 U.S.C. 331 (q) (2) and may be a violation of 18 U.S.C. 1001.

SECTION A

2. ESTABLISHMENT NAME

3. RECORD DATE *(Mo.)* *(Day)* *(Yr)*

4. NUMBER AND STREET

5. CITY

6. STATE

7. ZIP CODE

8. FOREIGN COUNTRY

9. ESTABLISHMENT TYPE *(See Instruction Booklet)*
D M R T S E O X G

SECTION B

10. OWNER/OPERATOR

11. OWNER/OPERATOR I.D.

12. NUMBER AND STREET

13. CITY

14. STATE

15. ZIP CODE

16. FOREIGN COUNTRY

17. TELEPHONE NUMBER - IF DIFFERENT FROM THAT OF OFFICIAL CORRESPONDENT
(Area Code) *(Number)*

SECTION C

18. OFFICIAL CORRESPONDENT

19. TELEPHONE NUMBER
(Area Code) *(Number)*

20. BUSINESS NAME

21. NUMBER AND STREET

22. CITY

23. STATE

24. ZIP CODE

25. FOREIGN COUNTRY

SECTION D

26. OTHER BUSINESS TRADING NAMES
(Enter any other name which the establishment in field #2 uses. Do not list Registered trademarks or names of private label distributors).

SEQ	ESTABLISHMENT NAME	SEQ	ESTABLISHMENT NAME
S01		S02	
S03		S04	

SECTION E

27. SIGNATURE OF OFFICIAL CORRESPONDENT

28. TITLE

FORM FDA 2891 (3/87)   PREVIOUS EDITIONS ARE OBSOLETE medical devices

Medical Device Establishment Registration

Information and Instructions

CENTER FOR
DEVICES AND
ADIOLOGICAL HEALTH
DRH

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
Public Health Service
Food and Drug Administration

IMPORTANT

Please read these new instructions carefully before completing the recently revised form FDA-2891, "Initial Registration of Medical Device Establishment." A sample of this form is enclosed for your reference. The completed form must be submitted within 30 days of entering into an operation which requires registration. If you are not yet in production, it is not necessary to register prior to submission of a 510(k) notification.

The official correspondent whom you delegate is responsible for all correspondence with the Food and Drug Administration (FDA) concerning registration and listing. Because this person is the official contact with FDA, it is important that you notify us of any changes immediately.

The official correspondent whom you delegate is responsible under 21 CFR 807.3(e) for:

a. completing the annual registration for the establishment;
b. maintaining contact with FDA for device listing;
c. maintaining and submitting a current list of officers and directors to FDA upon request of the Commissioner; and
d. receiving pertinent correspondence from FDA directed to and involving the owner or operator and/or any of the firm's establishments.

The completed FDA-2891 should be submitted to:

U.S. Food and Drug Administration
Center for Devices and Radiological Health
Device Registration and Listing Branch, HFZ-342
8757 Georgia Avenue
Silver Spring, Maryland 20910
Phone: (301) 427-7190

INSTRUCTIONS FOR COMPLETION OF THE INITIAL REGISTRATION OF MEDICAL DEVICE ESTABLISHMENT FORM (FDA-2891)

1. GENERAL INSTRUCTIONS

a. **Who Must Register.** Owners or operators of all device establishments, not exempt from the registration requirements (see **Who Is Not Required to Register**) that engage in the manufacture, preparation, propagation, compounding, assembly, or processing of a device intended for human use are required to register. The term "device" includes all in vitro diagnostic products and in vitro diagnostic biological products not subject to licensing under Section 351 of the Public Health Service Act (42 U.S.C. 262). Such owners or operators are required to register their principal place of business and all such establishments whether the ouptut of such establishments enter interstate commerce. The registration requirements shall pertain to any person who:

(1) initiates or develops specifications for a device which is to be manufactured by a second party for commercial distribution by the person initiating specifications;

(2) manufactures for commercial distribution a device either for himself or for another person (however, a person who only manufactures devices according to another person's specifications for commercial distribution by the person initiating specifications is not required to list those devices);

(3) repackages or relabels a device;

(4) initially distributes devices imported into the United States; or

(5) manufactures components or accessories that are ready to be used for any intended health-related purpose and are packaged or labeled for commercial distribution for such health-related purpose (e.g., blood filter, hemodialysis tubing) or devices that of necessity must be further processed by a licensed practitioner or other qualified person to meet the needs of a particular patient (e.g., manufacturer of ophthalmic lens blanks).

Foreign establishments are encouraged, but not required, to register.

b. **Who Is Not Required to Register.** The registration requirements do not pertain to:

(1) manufacturers of raw materials or components that are to be used in the manufacture or assembly of devices and who would otherwise not be required to register under the provisions of part 807.20;

(2) manufacturers or processors of devices to be used solely for veterinary purposes;

(3) manufacturers of general purpose articles, such as chemical reagents or laboratory equipment whose uses are generally known by persons trained in their use and that are not labeled or promoted for medical uses;

(4) licensed practitioners, including physicians, dentists, and optometrists, who manufacture or otherwise alter devices solely for use in their practice;

(5) pharmacies, surgical supply outlets, or other similar retail establishments dispensing or selling devices in the regular course of business at the retail level. This exemption also applies to those situations in which a pharmacy or other similar retail establisment purchases a device for subsequent distribution under its own name (e.g., a properly labeled health aid such as an elastic bandage, crutch, etc., indicating "distributed by" or "manufactured for" followed by the name of the pharmacy);

(6) persons who manufacture, prepare, propagate, compound, or process devices solely for use in research, teaching, or analysis and do not introduce such devices into commercial distribution;

(7) persons who handle devices but make no revisions to such devices or their immediate containers, such as wholesalers or warehousers;

(8) carriers by reason of their receipt, carriage, holding, or delivery of devices in the usual course of business as carriers; and

(9) persons who dispense devices to the ultimate consumer or whose major responsibility is to render a service necessary to provide a consumer with a previously manufactured device (e.g., a hearing aid dealer, optician, hospital, clinic, dental laboratory, clinical laboratory, etc.).

c. Definitions.

(1) Establishment - A place of business under one management at one general physical location at which a device is manufactured, assembled, or otherwise processed.

(2) Commercial distribution - Any distribution of a device intended for human use which is held or offered for sale, but not including: (i) internal or interplant transfer of a device between registered domestic establishments within the same parent, subsidiary, and/or affiliate company, or (ii) any distribution of a device intended for human use which has in effect an approved exemption for investigational use pursuant to section 520(g) of the Act.

(3) Manufacture, preparation, propagation, compounding, or processing of a device - The making by chemical, physical, biological, or other procedures of any articles that meet the definition of device as defined in Section 201(h) of the Act. These terms include the following activities: (i) repackaging or otherwise changing the container, wrapper, or labeling of any device package in furtherance of the distribution of the device from the original place of manufacture to the person who makes final delivery or sale to the ultimate consumer; (ii) initiation of specifications for devices that are manufactured by a second party for subsequent commercial distribution.

(4) Official Correspondent - The person desginated by the owner or operator of an establishment who is responsible for: (i) the annual registration of the establishment; (ii) contact with FDA for device listing; (iii) maintenance and submission of a current list of officers and directors to FDA upon request; (iv) the receipt of pertinent correspondence from FDA directed to and involving the owner or operator and/or any of the firm's establishments.

(5) Owner or operator - The corporation, subsidiary, affiliated company, partnership, or proprietor directly responsible for the activities of the registering establishment.

(6) Registration number - A unique number assigned by FDA to each establishment.

d. Misbranding by Reference to Establishment Registration or Establishment Registration Number. Registration of a device establishment or assignment of a registration number does not in any way denote approval of the establishment or its devices. Any representation that creates an impression of official approval because of registration or possession of a registration number is misleading and constitutes misbranding.

2. SPECIFIC INSTRUCTIONS FOR COMPLETION OF FORM FDA-2891

(Numbers in parentheses refer to the field number on the FDA-2891.)

(1) **Registration No.** Leave this space blank. FDA will assign a unique seven digit registration number to each establishment.

Section A. The purpose of this section is to obtain specific information on the registering establishment.

(2) **Establishment Name.** Enter the name of the establishment involved in registration activity and limit entry to 40 characters (abbreviate only if necessary).

(3) **Record Date.** Enter the month, day, and year the form is completed. All entries must be numeric and two characters each as shown below:

	Mo	Day	Yr
OCTOBER 7, 1987	10	07	87

(4) **Number and Street.** Enter the number and street at which the registering establishment is located. Do not use Postal Box or Rural Route numbers. Limit entry to 40 characters.

(5) **City.** Enter the city name in which the establishment is located. Limit entry to 20 characters.

(6) **State.** Enter the two-character State code of the U.S. Postal Service for the State, territory, or possession.

(7) **ZIP Code.** Enter the U.S. Postal ZIP Code.

(8) **Foreign Country.** Enter the foreign country name or abbreviation. Limit entry to 14 characters.

(9) **Establishment Type.** Space is provided for each designated code for establishment type. Select from the following descriptions the appropriate code or codes that reflect the device activity of the establishment. Enter the letter designation(s) in the spaces provided.

D Initial Distributor of Imported Devices - Takes first title to imported devices.

M Manufacturer - Makes by chemical, physical, biological, or other procedures, any article that meets the definition of device in section 201(h) of the Act.

R Repackager and/or Relabeler
Repackager - Packages finished devices from bulk or repackages devices made for the establishment by a manufacturer into different containers. (This does not include shipping containers.)

Relabeler - Changes the content of the labeling from that supplied from the original manufacturer for distribution under the establishment's own name. This does not include establishments that do not change the original labeling but merely insert their own name.

T Contract Sterilizer - Provides a sterilization service for another establishment's devices.

S Specification Developer - Develops specifications for a device that is distributed under the establishment's own name but performs no manufacturing.

E Contract Manufacturer - Manufactures a finished device to another establishment's specifications. The manufacturing establishment does not commercially distribute the device under its own name.

O Intermittent Manufacturer - Manufactures seasonally or periodically.

X Rebuilder/Refurbisher - Takes title to, refurbishes, or repairs devices to the original manufacturer's or the establishment's own specifications.

G Preproduction Registration - To be used only for registration prior to commencing actual production. This may not be used in conjunction with any other code. An establishment registration under this code is valid for only 1 year. If after 1 year, the establishment does not initiate an activity that requires registration, the registration will be cancelled.

Section B. The purpose of this section is to obtain information about the owner or operator of the establishment.

(10) **Owner/Operator.** Enter the business trading name of the corporation, subsidiary, affiliated company, partnership, or proprietor that is the owner or operator of the registering establishhment. Limit entry to 40 characters (abbreviate only if necessary).

(11) **Onwer/Operator I.D.** Leave this space blank. An identification number will be assigned to the owner/operator by FDA.

(12) **Number and Street.** Enter the number and street at which the owner or operator is located. Limit entry to 20 characters.

(13) **City.** Enter the city name in which the owner or operator is located. Limit entry to 20 characters.

(14) **State.** Enter the two-character State code of the U.S. Postal Service for the State, territory, or possession.

(15) **ZIP Code.** Enter the U.S. Postal ZIP Code.

(16) **Foreign Country.** Enter the name or abbreviation of the foreign country. Limit entry to 14 characters.

(17) **Telephone Number.** Enter an area code and telephone number only if it is different from that of the official correspondent.

Section C. The purpose of this section is to identify the individual designated as official correspondent. FDA may direct pertinent correspondence to the individual identified in this section.

(18) **Official Correspondent.** Enter the name of the individual designated as the official correspondent. The name must be printed or typed.

(19) **Telephone Number.** Enter the area code and telephone number of the official correspondent.

(20) **Business Name.** Enter the name of the establishment, owner or operator, or other place of business, as applicable, with which the official correspondent is associated.

(21) **Number and Street.** Enter the number and street of the official correspondent's place of business. Limit entry to 40 characters.

(22) **City.** Enter the city name in which the official correspondent's business is located. Limit entry to 20 characters.

(23) **State.** Enter the two-character State code of the U.S. Postal Service for the State, territory, or possession.

(24) **ZIP Code.** Enter the U.S. Postal ZIP Code.

(25) **Foreign Country.** Enter the name or abbreviation of the foreign country. Limit entry to 14 characters.

Section D. The purpose of this section is to record other names for this establishment that are used on device labels and that are different from the name under which the establishment is registering.

(26) **Establishment Name.** Enter each business trading name, using one block for each name. Limit entry in each block to 40 characters. Use an attached sheet if the number of names exceeds four. The business trading name is any other name by which the establishment labels their own device. The term does not include the names of distributors for whom this establishment makes devices. Do not list registered trademarks in use by the firm.

Section E. The signature (27) and title (28) of the designated official correspondent must appear in this section.

ADDRESSES OF FDA DISTRICT OFFICES

Address all requests for additional forms to the Registration Monitor at the following Food and Drug Administration District Offices:

Food and Drug Administration
1521 W. Pico Blvd.
Los Angeles, CA 90015
Phone: 213/252-7579

Food and Drug Administration
50 United Nations Plaza
San Francisco, CA 94102
Phone: 415/556-1456

Food and Drug Administration
721 19th St., Rm 500
U.S. Customhouse
Denver, CO 80202
Phone: 303/844-4915

Food and Drug Administration
7200 Lake Eleanor Dr., Ste 120
Orlando, FL 32809
Phone: 305/855-0900

Food and Drug Administration
60 8th St., NE
Atlanta, GA 30309
Phone: 404/347-4344

Food and Drug Administration
433 W. Van Buren St., Rm 1222
Chicago, IL 60607
Phone: 312/353-1829

Food and Drug Administration
4298 Elysian Fields Ave.
New Orleans, LA 70122
Phone: 504/589-6345

Food and Drug Administration
424 Trapelo Rd., Bldg 104
Waltham, MA 02154
Phone: 617/647-8132

Food and Drug Administration
900 Madison Ave.
Baltimore, MD 21201
Phone: 301/962-3396

Food and Drug Administration
1560 E. Jefferson Ave.
Detroit, MI 48207
Phone: 313/226-6260

Food and Drug Administration
240 Hennepin Ave.
Minneapolis, MN 55401
Phone: 612/349-3952

Food and Drug Administration
1009 Cherry St.
Kansas City, MO 64106
Phone: 816/374-5623

Food and Drug Administration
20 Evergreen Pl.
East Orange, NJ 07018
Phone: 201/645-6230

Food and Drug Administration
850 Third Ave.
Brooklyn, NY 11232
Phone: 718/965-5275

Food and Drug Administration
599 Delaware Ave.
Buffalo, NY 14202
Phone: 716/846-4474

Food and Drug Administration
1141 Central Pkwy.
Cincinnati, OH 45202
Phone: 513/684-3505

Food and Drug Administration
2nd & Chestnut Sts., Rm 900
Philadelphia, PA 19106
Phone: 215/597-4345

Food and Drug Administration
297 Plus Park Blvd.
Nashville, TN 37217
Phone: 615/736-5079

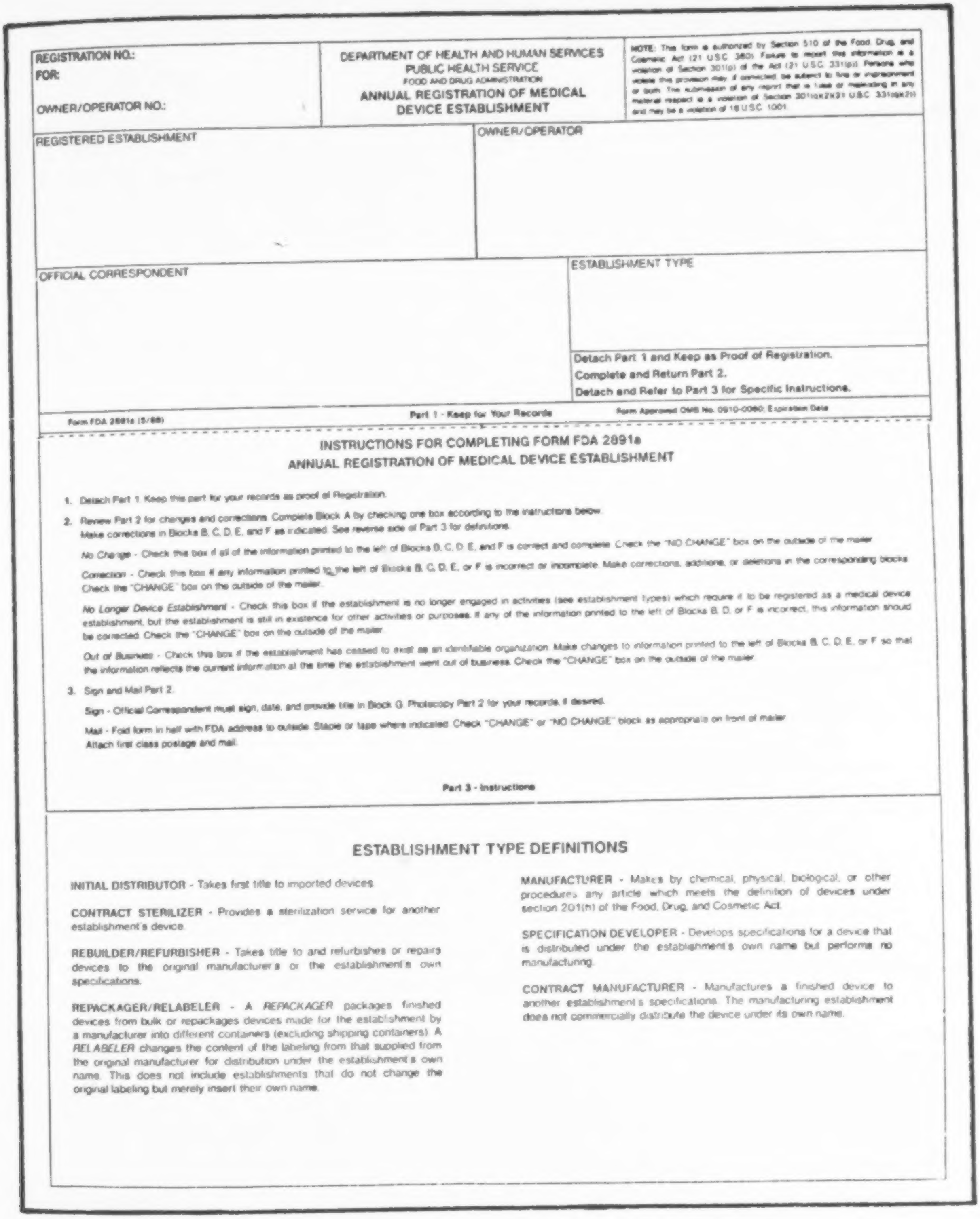
Food and Drug Administration
3032 Bryan St.
Dallas, TX 75204
Phone: 214/767-0312

Food and Drug Administration
909 1st Ave., Fed Ofc Bldg 5009
Seattle, WA 98174
Phone: 206/442-5300

Food and Drug Administration
P.O. Box 4427, San Juan Sta.
San Juan, PR 00905
Phone: 809/723-4895

HHS Publication (FDA) 87-4199
May 1987

ANNUAL REGISTRATION FORM
(FDA 2891a)



REGISTRATION NO.:
FOR:

OWNER/OPERATOR NO.:

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION
ANNUAL REGISTRATION OF MEDICAL DEVICE ESTABLISHMENT

NOTE: This form is authorized by Section 510 of the Food, Drug, and Cosmetic Act (21 U.S.C. 360). Failure to report this information is a violation of Section 301(p) of the Act (21 U.S.C. 331(p)). Persons who violate this provision may, if convicted, be subject to fine or imprisonment or both. The submission of any report that is false or misleading in any material respect is a violation of Section 301(q)(2)(21 U.S.C. 331(q)(2)) and may be a violation of 18 U.S.C. 1001.

REGISTERED ESTABLISHMENT

OWNER/OPERATOR

OFFICIAL CORRESPONDENT

ESTABLISHMENT TYPE

Detach Part 1 and Keep as Proof of Registration.
Complete and Return Part 2.
Detach and Refer to Part 3 for Specific Instructions.

Form FDA 2891a (5/88) **Part 1 - Keep for Your Records** Form Approved OMB No. 0910-0060; Expiration Date

INSTRUCTIONS FOR COMPLETING FORM FDA 2891a
ANNUAL REGISTRATION OF MEDICAL DEVICE ESTABLISHMENT

1. Detach Part 1. Keep this part for your records as proof of Registration.
2. Review Part 2 for changes and corrections. Complete Block A by checking one box according to the instructions below. Make corrections in Blocks B, C, D, E, and F as indicated. See reverse side of Part 3 for definitions.

   No Change - Check this box if all of the information printed to the left of Blocks B, C, D, E, and F is correct and complete. Check the "NO CHANGE" box on the outside of the mailer.

   Correction - Check this box if any information printed to the left of Blocks B, C, D, E, or F is incorrect or incomplete. Make corrections, additions, or deletions in the corresponding blocks. Check the "CHANGE" box on the outside of the mailer.

   No Longer Device Establishment - Check this box if the establishment is no longer engaged in activities (see establishment types) which require it to be registered as a medical device establishment, but the establishment is still in existence for other activities or purposes. If any of the information printed to the left of Blocks B, D, or F is incorrect, this information should be corrected. Check the "CHANGE" box on the outside of the mailer.

   Out of Business - Check this box if the establishment has ceased to exist as an identifiable organization. Make changes to information printed to the left of Blocks B, C, D, E, or F so that the information reflects the current information at the time the establishment went out of business. Check the "CHANGE" box on the outside of the mailer.
3. Sign and Mail Part 2.

   Sign - Official Correspondent must sign, date, and provide title in Block G. Photocopy Part 2 for your records, if desired.

   Mail - Fold form in half with FDA address to outside. Staple or tape where indicated. Check "CHANGE" or "NO CHANGE" block as appropriate on front of mailer. Attach first class postage and mail.

Part 3 - Instructions

ESTABLISHMENT TYPE DEFINITIONS

INITIAL DISTRIBUTOR - Takes first title to imported devices.

CONTRACT STERILIZER - Provides a sterilization service for another establishment's device.

REBUILDER/REFURBISHER - Takes title to and refurbishes or repairs devices to the original manufacturer's or the establishment's own specifications.

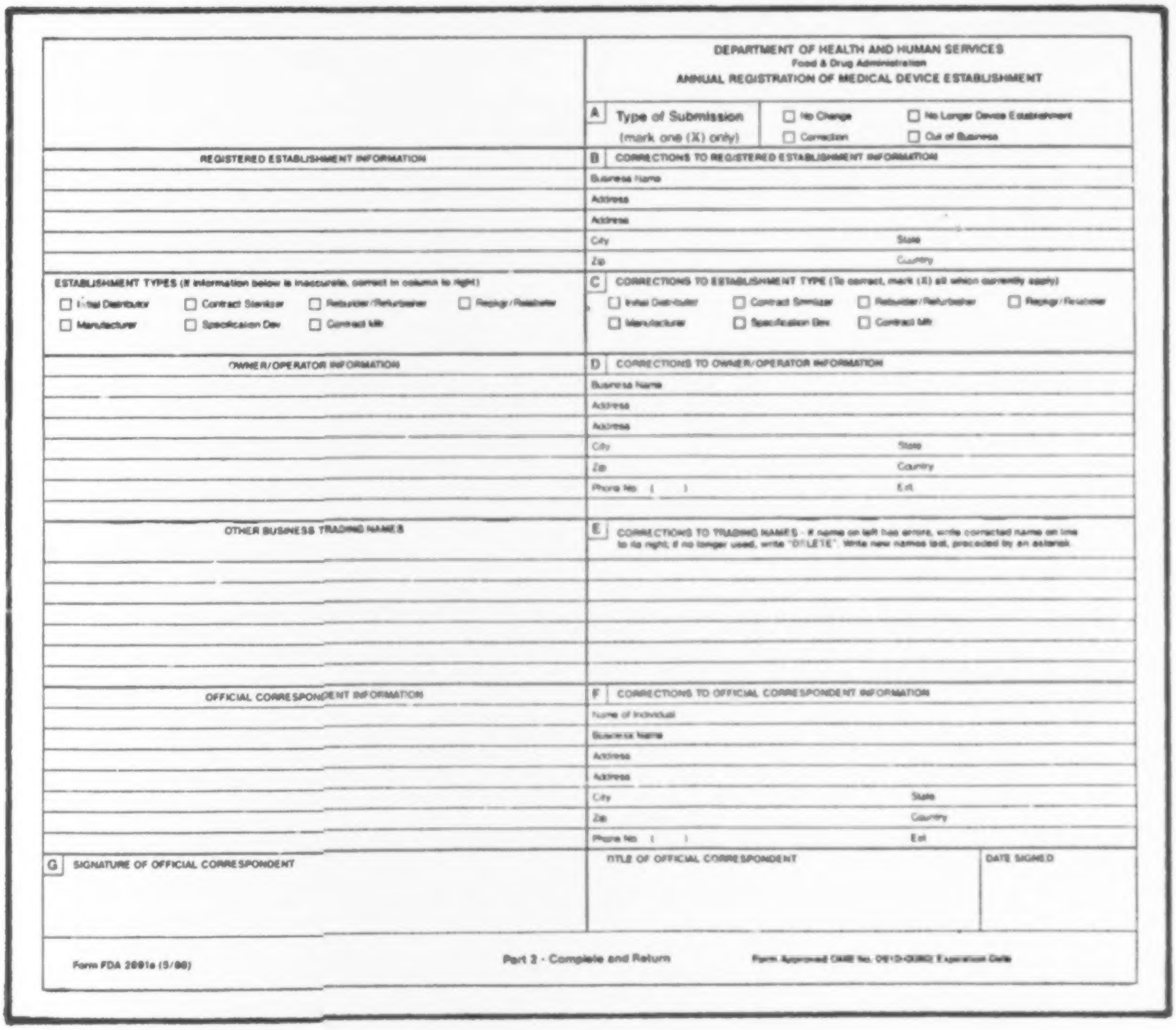
REPACKAGER/RELABELER - A *REPACKAGER* packages finished devices from bulk or repackages devices made for the establishment by a manufacturer into different containers (excluding shipping containers). A *RELABELER* changes the content of the labeling from that supplied from the original manufacturer for distribution under the establishment's own name. This does not include establishments that do not change the original labeling but merely insert their own name.

MANUFACTURER - Makes by chemical, physical, biological, or other procedures any article which meets the definition of devices under section 201(h) of the Food, Drug, and Cosmetic Act.

SPECIFICATION DEVELOPER - Develops specifications for a device that is distributed under the establishment's own name but performs no manufacturing.

CONTRACT MANUFACTURER - Manufactures a finished device to another establishment's specifications. The manufacturing establishment does not commercially distribute the device under its own name.

ANNUAL REGISTRATION FORM
(FDA 2891a)
(continued)



DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food & Drug Administration
ANNUAL REGISTRATION OF MEDICAL DEVICE ESTABLISHMENT

A Type of Submission (mark one (X) only)
☐ No Change ☐ No Longer Device Establishment
☐ Correction ☐ Out of Business

REGISTERED ESTABLISHMENT INFORMATION

ESTABLISHMENT TYPES (If information below is inaccurate, correct in column to right)
☐ Initial Distributor ☐ Contract Sterilizer ☐ Rebuilder/Refurbisher ☐ Repkgr/Relabeler
☐ Manufacturer ☐ Specification Dev ☐ Contract Mfr

OWNER/OPERATOR INFORMATION

OTHER BUSINESS TRADING NAMES

OFFICIAL CORRESPONDENT INFORMATION

B CORRECTIONS TO REGISTERED ESTABLISHMENT INFORMATION
Business Name
Address
Address
City State
Zip Country

C CORRECTIONS TO ESTABLISHMENT TYPE (To correct, mark (X) all which currently apply)
☐ Initial Distributor ☐ Contract Sterilizer ☐ Rebuilder/Refurbisher ☐ Repkgr/Relabeler
☐ Manufacturer ☐ Specification Dev ☐ Contract Mfr

D CORRECTIONS TO OWNER/OPERATOR INFORMATION
Business Name
Address
Address
City State
Zip Country
Phone No ( ) Ext

E CORRECTIONS TO TRADING NAMES - If name on left has errors, write corrected name on line to its right; if no longer used, write "DELETE". Write new names last, preceded by an asterisk.

F CORRECTIONS TO OFFICIAL CORRESPONDENT INFORMATION
Name of Individual
Business Name
Address
Address
City State
Zip Country
Phone No ( ) Ext

G SIGNATURE OF OFFICIAL CORRESPONDENT

TITLE OF OFFICIAL CORRESPONDENT

DATE SIGNED

Form FDA 2891a (5/90) Part 2 - Complete and Return Form Approved OMB No. 0910-0082 Expiration Date

4 MEDICAL DEVICE LISTING

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INTRODUCTION

Section 510 of the Act requires that manufacturers list medical devices in commercial distribution in the U.S. with the Food and Drug Administration (FDA). Manufacturers of medical devices are required to list their devices by generic category (classification name) on Form FDA 2892. However, only initial distributors in lieu of submitting FDA-2892(s) are required to submit the classification name for each imported device and the name and address of the foreign manufacturer. In addition, manufacturers must maintain an historical listing file in accord with 807.31 containing labeling and advertisements.

Neither registration nor listing constitutes FDA clearance or approval for marketing or commercial distribution. Unless exempt, a premarket notification submission [510(k)] or a premarket approval application (PMA) is required prior to commercial distribution.

WHO MUST LIST

The following categories of firms commercially distributing medical devices must list by submitting a Form FDA 2892:

- manufacturers of finished medical devices;
- manufacturers of components or accessories sold to the end-user;
- specification developers;
- repackagers and relabelers;
- foreign manufacturers or exporters; and
- initial distributors engaged in specification development and/or repackaging or relabeling activities.

Those foreign manufacturers for which there exists joint ownership and control with a domestic establishment may have the domestic establishment submit listing information and maintain the historical file of labeling and advertisements.

Foreign manufacturers exporting devices into the U.S. for which there is no domestic joint ownership and control may comply with the listing requirement by authorizing their sole initial distributor to complete the Form FDA 2892 on their behalf. A sole initial distributor is an "exclusive distributor for a foreign manufacturer;" that is, he is the only initial distributor in the U.S. importing devices from a specific manufacturer.

Initial distributors so authorized must:

- o be the sole initial distributor of the device(s) listed;
- o maintain a labeling and advertisement historical file for the device(s); and
- o provide FDA with the foreign firm's letter of authorization, along with listing Form(s) FDA 2892.

The following categories of firms required to register are not required to list on Form FDA 2892:

- o contract manufacturers;
- o contract sterilizers; and
- o initial distributors **not** engaged in specification development and/or repackaging or relabeling activities.

HOW TO LIST

Listing of a device is done by completing Form FDA 2892, "Medical Device Listing." To aid in completing this form, FDA provides three booklets: "Medical Device Listing, Information and Instructions;" "Classification Names for Medical Devices;" and "Classification Names for In Vitro Diagnostic Products." The first publication, "Medical Device Listing, Information and Instructions," contains an overview of the listing process, specific instructions for completing the form, and several examples of properly completed forms. A copy of this booklet is included in this chapter. The other two booklets contain the classification names and 5 character codes to complete items 8 and 9 on Form FDA 2892.

WHEN TO LIST

A properly completed Form FDA 2892 must be submitted within 30 days of receipt of the listing material from the FDA for devices in commercial distribution. However, a properly completed form must be submitted by the foreign manufacturer or their **sole** initial distributor before their medical device can be imported into the U.S. Otherwise, foreign-made devices may be detained.

WHERE TO SUBMIT

All but the bottom or yellow copy of Form FDA 2892 should be submitted to the following address:

Device Registration and Listing Branch (HFZ-342)
Center for Devices and Radiological Health
Food and Drug Administration
5600 Fishers Lane
Rockville, Maryland 20857

The listing firm should keep the bottom copy of the form because, unlike registration, no validated copy of the Form FDA 2892 is returned to the submitter. The bottom copy of the Form FDA 2892 retained by the submitter is proof of listing. FDA may contact the submitter for clarification of data or return incorrect forms for resubmission. FDA will not return the bottom copy of the form to the submitter.

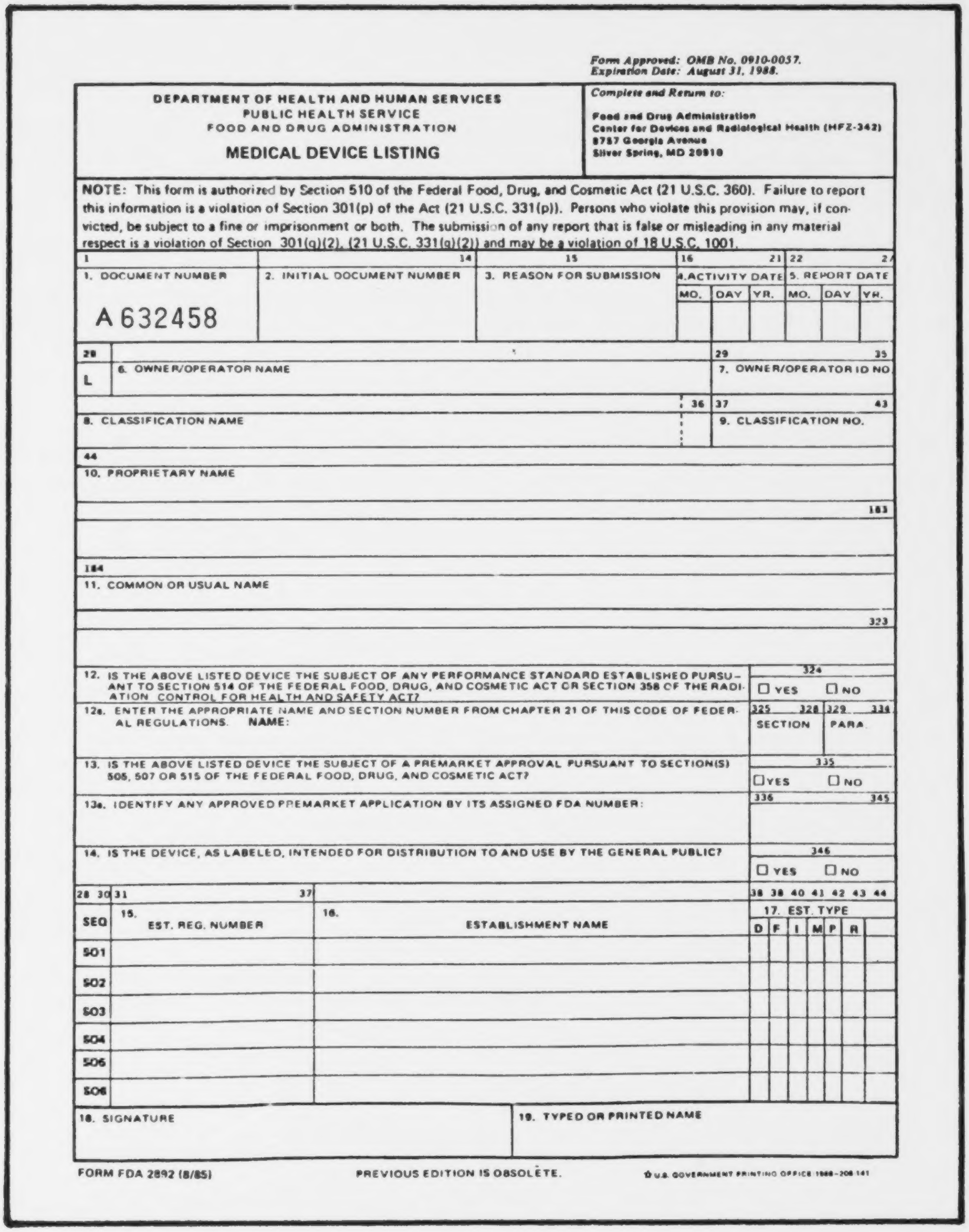
UPDATING LISTING DATA

Firms required to list are responsible for keeping current the data on their FDA 2892. Unlike establishment registration, device listing data is updated by entering the corrected information on a "new" Form FDA 2892. Device listing data must be updated at the firm's discretion when one or more of the following occurs:

- a "new" device is marketed with a classification name that is not currently listed;
- the intended use of a listed device changes in such a way that would result in its being more appropriately classified under a different generic category (classification name);
- the marketing of all models or variations of the listed device is discontinued;
- a device previously discontinued is re-marketed; or
- any of the information changes that must be supplied on Form FDA 2892, other than changes in proprietary and common or usual name.

best copy available

MEDICAL DEVICE LISTING
(FDA 2892)



Form Approved: OMB No. 0910-0057.
Expiration Date: August 31, 1988.

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION

MEDICAL DEVICE LISTING

Complete and Return to:

Food and Drug Administration
Center for Devices and Radiological Health (HFZ-342)
8757 Georgia Avenue
Silver Spring, MD 20910

NOTE: This form is authorized by Section 510 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 360). Failure to report this information is a violation of Section 301(p) of the Act (21 U.S.C. 331(p)). Persons who violate this provision may, if convicted, be subject to a fine or imprisonment or both. The submission of any report that is false or misleading in any material respect is a violation of Section 301(q)(2), (21 U.S.C. 331(q)(2)) and may be a violation of 18 U.S.C. 1001.

1	14	15	16		21	22		2
1. DOCUMENT NUMBER	2. INITIAL DOCUMENT NUMBER	3. REASON FOR SUBMISSION	4. ACTIVITY DATE			5. REPORT DATE		
			MO.	DAY	YR.	MO.	DAY	YR.
A 632458								

28 L — 6. OWNER/OPERATOR NAME
29 — 35 — 7. OWNER/OPERATOR ID NO.

36 — 8. CLASSIFICATION NAME
37 — 43 — 9. CLASSIFICATION NO.

44 — 10. PROPRIETARY NAME — 183

184 — 11. COMMON OR USUAL NAME — 323

12. IS THE ABOVE LISTED DEVICE THE SUBJECT OF ANY PERFORMANCE STANDARD ESTABLISHED PURSUANT TO SECTION 514 OF THE FEDERAL FOOD, DRUG, AND COSMETIC ACT OR SECTION 358 OF THE RADIATION CONTROL FOR HEALTH AND SAFETY ACT? (324) ☐ YES ☐ NO

12a. ENTER THE APPROPRIATE NAME AND SECTION NUMBER FROM CHAPTER 21 OF THIS CODE OF FEDERAL REGULATIONS. NAME: (325 — 328) SECTION (329 — 334) PARA.

13. IS THE ABOVE LISTED DEVICE THE SUBJECT OF A PREMARKET APPROVAL PURSUANT TO SECTION(S) 505, 507 OR 515 OF THE FEDERAL FOOD, DRUG, AND COSMETIC ACT? (335) ☐ YES ☐ NO

13a. IDENTIFY ANY APPROVED PREMARKET APPLICATION BY ITS ASSIGNED FDA NUMBER: (336 — 345)

14. IS THE DEVICE, AS LABELED, INTENDED FOR DISTRIBUTION TO AND USE BY THE GENERAL PUBLIC? (346) ☐ YES ☐ NO

28 30	31 37		38	39	40	41	42	43	44
			17. EST. TYPE						
SEQ	15. EST. REG. NUMBER	16. ESTABLISHMENT NAME	D	F	I	M	P	R	
501									
502									
503									
504									
505									
506									

18. SIGNATURE
19. TYPED OR PRINTED NAME

FORM FDA 2892 (8/85) PREVIOUS EDITION IS OBSOLETE. ☆ U.S. GOVERNMENT PRINTING OFFICE 1986-208-141 medical devices

CENTER FOR
DEVICES AND
RADIOLOGICAL HEALTH

Medical Device Listing Information and Instructions

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
Public Health Service
Food and Drug Administration

GENERAL AND SPECIFIC INSTRUCTIONS FOR COMPLETING THE DEVICE LISTING FORM FD-2892

Section 510(j) of the Federal Food, Drug and Cosmetic Act requires that each person who must register his establishment according to Sections 510(b), (c), or (d) is also required to submit a list of devices which he manufactures, prepares, propagates, compounds, or processes. This list shall be submitted in the form and manner prescribed by the Commissioner. Provisions are also made in Section 510(j)(1)(A&B) for submission of additional information along with the device listings. (See Appendix II for Pertinent Portions of the Act.)

Form FD-2892 (Medical Device Listing) is the form to be used for the initial listing of devices and subsequent updating of device listing information. The FDA is requiring that each owner/operator select the classification name of the device from the list of classification names provided with the instructions. This list contains terms used by FDA's Classification Panels to classify devices into regulatory control categories. The use of classification names will facilitate the collection, organization, and retrieval of listing information.

At this time, FDA is not requiring that all labels, package inserts, other labeling, and advertisements be submitted with each device listed. Instead, each owner/operator must make available upon request all labels and labeling for Class II (Performance Standards) and Class III (Premarket Approval) devices, labeling and advertisements for each restricted device (21 CFR - Paragraph 807.3(i)), and all labels, package inserts and a representative sample of any other labeling for each Class I (General Controls) device. Submitting this information in response to a request is intended to provide the Agency, on an as needed basis, information regarding chronological changes made in labels, package inserts, other labeling and advertising.

B. GENERAL INSTRUCTIONS

1. Special Listing Procedures.

a. Initial Distributors of Foreign Devices. Each owner/operator who initially distributes foreign-made devices (except those devices for which he has developed specifications) shall not submit Form FD-2892 for the foreign devices he distributes in the United States. Instead he shall meet the requirements of the regulation. (21 CFR- Paragraph 807.22)

An initial distributor of a foreign device owner/operator may submit a listing on behalf of that owner/operator only if:

(i) he is the only domestic distributor of that foreign owner/operator's devices, and;

(ii) he submits to FDA a letter from the foreign owner/operator authorizing the initial distributor to list on his behalf and maintain the required Historical Listing File.

b. Specification Developers. Each owner/operator who develops specifications and has the devices manufactured for himself by other owner/operators must list those devices. An owner/operator who manufacturers devices according to other owner/operator specifications only are not required to list those devices.

2. Times for Submitting and Updating Device Listing. (21 CFR paragraph 807.21)

a. Initial Listing: An owner/operator who has not submitted an initial listing of devices shall do so within 30 days of receipt of the listing material from Bureau of Medical Devices. Listing material is sent to the owner/operator of a newly registered establishment.

An owner/operator who introduces a new device to commercial distribution must list that device during the next update period in June or December.

b. When to Update: The owner/operator is required to update twice a year during the months of June and December or at his discretion at the time the change occurs as defined in the regulation. (21 CFR paragraph 807.30).

c. Changes Requiring Updating.

(1) A device is introduced into commercial distribution and a device of the same classification name is not currently listed with FDA.

(2) All devices of the same classification name are discontinued.

(3) A change occurs in one or more but not all of multiple classification names reported for the same device (Appendix I- Example 16), or for classified accessories, components, or parts.

(4) A change occurs in Blocks 6,7, and 12 thru 17 on Form FD-2892

(5) Commercial distribution of devices identified by a previously discontinued classification name is resumed

c. Changes not requiring updating.

(1) field 36 of Block 8

(2) proprietary names

(3) common or usual names

(4) supplemental lists or catalog pages of unclassified components, parts, or accessories.

(5) changes in any labeling submitted with a Form FD-2892

e. Updating Procedure.

(1) Form FD-2892 (Medical Device Listing) is used to update previously submitted device listing information.

(2) Initial Document Number. Enter in Block 2 of Form FD-2892 the preprinted number that appears on the original form FD-2892 on which the device was listed and which you desire to update.

(3) Reason for Submission. Select the appropriate code from the list under (3) on page 8.

(4) Refer to examples #14 to #18 for proper format in completion of Form FD-2892.

3. Where to List Devices. (21 CFR- Paragraph 807.22)

4. Historical Listing File.

a. Maintenance of the Historical Listing File. Each owner/operator is required to maintain a historical listing file. (21 CFR - Paragraph 807.31). The regulations do not provide specific procedures for the maintenance of the file.

b. FDA Requests for Information from the Historical Listing File. Upon request by FDA, the owner/operator will be required to submit copies of a portion or all of the materials contained in the historical listing file.

5. Classification Lists.

FDA's Classification Panels have assembled a list of devices that are tentatively classified into regulatory control categories.

The Classification Panels are organized according to the following 19 medical speciality panels as follows:

Code	Device Panel	Code	In Vitro Products Panel
73	Anesthesiology	75	Chemistry
74	Cardiovascular	81	Hematology
76	Dental	82	Immunology
77	Ear, Nose & Throat	83	Microbiology
78	Gastroenterology and Urology	88	Pathology
79	General & Plastic Surgery	91	Toxicology
80	General Hospital		
84	Neurology		
85	Obstetrics and Gynecology		
86	Ophthalmic		
87	Orthopedics		
89	Physical Medicine		
90	Radiology		

All of the devices classified by the above 19 panels have been placed on two "keyword" classification lists. The Medical Device Keyword List contains devices classified by the first 13 panels. The In Vitro Diagnostic keyword list contains all in vitro diagnostic products classified by the remaining 6 panels.

The keyword lists were developed by listing a name under each of the pertinent words within the name of the device. For example: 1) an operating room table can be found on the keyword list under "Operating," "Room," and "Table," and 2) the in vitro diagnostic flame photometry method for the detection of sodium can be found on the keyword list under "Sodium Analysis Products."

No significance should be placed on the specialty panel which classified a specific device. Devices were assigned to the panel that would be most familiar with a particular device. For instance, an owner/operator promotes a device for orthopedic purposes. He finds that it has been classified by the Neurology Panel. The owner/operator would, therefore, use the classification name and number assigned by the Neurology Panel.

There are some instances in which a device was, in fact, classified by more than one panel. Only in those cases will the owner/operator take into consideration his labeled or promotional claims in order to select the correct classification names. (Appendix I - Example 6)

The definition of "device" in Section 201(h) of the Act includes components, parts, or accessories. During FDA's classification of devices, related items such as components, parts, and accessories were generally included with the devices. For example, Electrosurgical Cutting and Coagulation Devices and Accessories, are found on the list of devices classified by the General and Plastic Surgery Panel.

Another approach used by the panels can be found on the list of devices classified by the Physical Medicine Panel. The panel classified 5 types of wheelchairs. Also found on the keyword list under "wheelchair" are 19 wheelchair accessories.

A third approach can be found on the list of devices classified by the Anesthesiology Panel. Under "Gas" are found 19 gas analyzers. In this third example, accessories are not specifically mentioned.

In all three cases, it was expected that components, parts, and accessories including replacement items would be marketed separately to purchasers of electrosurgical cutting and coagulation devices, wheelchairs, and gas analyzers .

FDA has determined that it is not necessary in all cases to identify on listing forms each unclassified component, part, or accessory separately marketed in support of a device. This is further discussed in Part 6 below.

6. How to List Your Device.

A. Introduction

We suggest that you first list each "stand alone" device you market. A "stand alone" device is considered a marketed unit or system that is promoted and sold for a health related purpose. It is not marketed as a component, part or accessory for another device. Such a device may range from a simple surgical instrument to an intensive care monitoring system.

Proceed to identify a classification name for each marketed device or system. Any device classification name on the list for which there are minor variations in size, packaging, shape, components, etc. that do not alter the intended use of the device are to be consolidated onto one Form FD-2892. For example needles in different gauges, lengths, or package sizes would be listed on one Form FD-2892. (Appendix I - Examples 2, 3)

B. Select a Classification Name for "Stand Alone" Device

For each marketed "stand alone" device, select a classification name from the appropriate classification list. NOTE: Some panels classified the systems or collection of devices while other panels classified only components. Proceed as follows:

(i) If you can select a name that identifies the "stand alone" device such as dental x-ray system, fetal electroencephalograph (and accessories), forceps, etc., enter that name in Block 8 of Form FD-2892.

(ii) If you can identify more than one name for the "stand alone" device, enter the word "MULTIPLE" in Block 8 of Form FD-2892 and include the classification names and numbers on a supplemental sheet under the heading "DEVICE NAMES".

(iii) If you cannot identify a classification name for the "stand alone" device enter the word "NONE" in Block 8 of Form FD-2892 and also the name of the classification panel which would classify the device. (The names of the classification panels are found on the first page of each classification list).

C. Identifying Classified Components, Parts, and Accessories for Devices You Manufacture, Package or Label

If for the device listed on Form FD-2892, you also market components, parts, or accessories which you manufacture, package, or label identify them as follows:

(i) Enter on a supplemental sheet under the heading "RELATED ITEMS," the classification name and number or each components, part, or accessory that can be identified on a classification list. If, in addition, you market components, parts, or accessories which do not appear on the classification list, enter the letter "R" in field 36 of Block 8 of Form FD-2892.

(ii) If, in addition, to marketing classified and unclassified components, parts, and accessories for the device being listed you also market such related items for another owner/operator's device, enter the letter "B" (or the letter "B" instead of the letter "R") in field 36 of Block 8 on Form FD-2892.

D. Identifying Components, Parts, and Accessories Marketed Only for Other Owner/Operator's Devices

If you manufacture, package, or label components, parts or accessories only for another owner/operator's "stand alone" device, select a classification name for that "stand alone" device as directed in Step B. In addition, enter the letter "O" in field 36 of Block 8 on Form FD-2892, and identify your components, parts, or accessories as directed in Step C. (Appendix I - Example 11)

7. Special Situations

Certain devices require further instructions to aid in listing.

a. Device Kits. Certain "stand alone" devices being listed will be "kits," "trays," or "sets," etc. For example, a "lumbar puncture kit" contains syringes, specimen collection tubes, drapes, spinal needle, etc. In those situations where the kit is not on the classification list, follow Rule "c" on page 9 of the Specific Instructions for completing Block 8 on Form FD-2892. However, do not assign classification names and numbers to each item contained in the "kit." (Appendix I - Example 8)

b. Transitional Devices. Some devices are currently being regulated as drugs which require approved "New Drug Applications" (NDA) or "Antibiotic Forms 5 or 6"; e.g., absorbable sutures, soft contact lenses, antibiotic sensitivity disks, etc. These devices which are required to be listed as drugs must also be listed as devices. The Form FD-2892 must include in Block 11 the National Drug Code (NDC) numbers assigned to the transitional device. (Appendix I - Example 4)

c. Devices Included with Drug Packages. Manufacturers who include devices as part of drug packages for the purpose of administering the drug (such as calibrated droppers, prefilled syringes, etc.) are not to list those devices but must insure that these accessories have been listed with the Bureau of Drugs as instructed for completing Form FD-2657 (Drug Product Listing).

d. Questionable Devices. There will be situations when an owner/operator questions whether or not his product is considered a medical device subject to listing. We recommend that he submit a letter including labeling adequate to describe the device and request a determination as to whether or not the product is considered a device. Submit this letter of inquiry to the address appearing on Form FD-2892.

C. SPECIFIC INSTRUCTIONS FOR COMPLETING FORM FD-2892 (MEDICAL DEVICE LISTING).

1. Introduction

All of the information provided on Form FD-2892 must be in English. When necessary, a supplemental sheet can be used to complete or clarify your submission. Supplemental sheets must be letter size and contain in the upper right hand corner the preprinted document number for that submission.

Any material(s) submitted for listing purposes (i.e., labeling, catalog pages, etc.) must have the document number for that submission entered on each separate item or be attached to a supplemental sheet.

2. Completion of Form FD-2892.

(Numbers in parenthesis correspond to block numbers on FD-2892.)

FDA's control of all listing submissions will be based upon the preprinted document number in Block 1 of each Form FD-2892. When a device is listed for the first time, a record must be made of this initial document number for future reference. Form FD-2892 is a three-part form. The third (yellow) copy serves as a file copy for the owner/operator.

Upon completion of the form, detach this yellow copy and retain as a record of listing.

Return the two white copies with the listing submission. Any correspondence relating to a specific listing form must reference its document number. The document number is not to be interpreted as a licensing or approval number and it shall not be used on device labeling.

(1) Document Number

Preprinted number.

(2) Initial Document Number

If your submission refers to a previously listed device as in the case of an update, the document number of the initial submission must be provided in Block 2. If this is an initial submission, leave Block 2 blank.

(3) Reason for Submission

Select from the following list the appropriate reason for submission and enter the corresponding letter in Block 3.

LETTER	REASON FOR SUBMISSION
A	Initial device listing (owner/operator listing all his devices for the first time)
B	Adding a classification name not previously listed
C	Change, correction, or deletion to previously submitted information (This includes an addition or deletion of one or more but not all classification names when multiple classification names were initially listed.)
D	Discontinuance of a previously listed classification name
R	Resumption of a previously discontinued classification name

(4) Activity Date

The approximate date when the reason for submission (as indicated in Block 3) occurred. All entries in Block 4 must be numerical and have two (2) characters for each entry of the month, day, and year. For an initial listing, this block may be left blank.

EXAMPLE: March 1, 1977, would be entered:

MO	DAY	YR
03	01	77

(5) Report Date

The actual date that Form FD-2892 was completed. Enter this date in Block 5 using the same format illustrated in the example for Block 4.

(6) Owner/Operator Name

Enter in Block 6 the business trading name of the corporation, subsidiary, affiliated company, partnership, or proprietor that is responsible for completing and submitting the device listing information. When applicable, this name should be the same as that was entered in Block 11 on Form FD-2891, "Initial Registration of Medical Device Establishment" or Line 8 of Form FD-2891(a), "Annual Registration of Medical Device Establishment."

(7) Owner/Operator ID

Enter in Block 7 the seven-digit number assigned to the owner/operator when the establishment registered with FDA. The owner/operator ID is located in Block 12 of Form FD-2891, - "Initial Registration of Medical Device Establishment" and line 7 of Form FD-2891(a) - "Annual Registration of Medical Device Establishment."

Each domestic owner/operator who has not registered must first do so for the purpose of obtaining owner/operator ID and registration numbers. Foreign establishments that are not registered will enter "FOREIGN" in Block 7.

(8) Classification Name

Before selecting a classification name review the "General Instructions" with special attention to Parts 5, 6, and 7. Select the noun term in any name as the first keyword, i.e., if listing a piston syringe, select the word syringe as the first keyword. If the term you select as the keyword cannot be located in the keyword list, select another term. When entering classification names, use abbreviations when necessary. It is important that FDA be able to verify the classification name and corresponding number.

Complete Block 8 in accordance with one of the following rules:

(a) Single Name Selected From List. Enter the name selected from the classification list. On a supplemental sheet under the heading "RELATED ITEMS" include the classification names and numbers of any manufactured, packaged, or labeled components, parts, or accessories marketed separately in support of the listed device. (Appendix I - Examples 1, 5, 7, 9, 12)

Do not include any labels, labeling or other information for the device or classified related items.

(b) Multiple Names Selected From List. If the device or system can be described by two or more names from the list, enter the word "MULTIPLE" in Block 8. On a supplemental sheet under the heading "DEVICE NAMES" include the classification names and numbers. If appropriate on the supplemental sheet, include under the heading "RELATED ITEMS" the classification names and numbers of any manufactured, packaged, or labeled components, parts, or accessories marketed separately in support of the listed device. (Appendix I - Example 6)

Do not include any labels, labeling or other information for the classified devices or classified related items.

(c) No Name Selected From List. Enter the word "NONE" in Block 8 on Form FD-2892. On a supplemental sheet under the heading

"RELATED ITEMS" include the classification names and numbers of any manufactured, packaged, or labeled component, parts, or accessories marketed separately in support of the device. Also identify any unclassified components, parts, or accessories by including appropriate annotated catalog pages. (Appendix I - Example 10)

Attach minimum labeling or other descriptive information such as specification sheets, catalog descriptions, etc. adequate to describe the device and its intended use.

(8) - Field 36

This field located at the right of Block 8 is to be used to identify manufactured, packaged, or labeled components, parts or accessories marketed in support of a "stand alone" device. This field is to be completed only when listing a device following rules (a) and (b) above. Select the appropriate code from the following list.

Letter	Activity
B	Markets classified and unclassified components, parts, or accessories for your own and also for another owner/operator's "stand alone" device.
O	Markets classified or unclassified components, parts, or accessories only for another owner/operator's "stand alone" device.
R	Markets unclassified components, parts or accessories only for own device.

(9) Classification Number

Enter the five character code from the classification list that corresponds to the classification name you have selected. If you entered "MULTIPLE" or "NONE" in Block 8, leave this block blank.

(10) Proprietary Name

Enter the proprietary name (trade or catalog name) of the device. Use only those abbreviations in the proprietary name that appear on the label or labeling. Exclude as part of the device proprietary name any reference to physical characteristics such as size, package shape, or color. If more than one proprietary name is used for the device or devices being listed, enter "MULTIPLE" in Block 10.

(11) Common or Usual Name

FDA recognizes that no "established names" for devices have been designated pursuant to Section 508 of the Act and that few "official titles" for devices are recognized in an official compendium. Consequently, the common or usual name must be provided in order to satisfy the listing requirement. The common or usual name can be any descriptive phrase and does not have to have industry wide or user acceptance.

If the common or usual name is the same as that entered for the proprietary name, enter "SAME" in Block 11

If more than one device is being listed under one classification name, enter a descriptive phrase which represents the group of devices i.e., "Various Types of Rongeurs," or "Various Models of X-Ray Systems." (Appendix I - Examples 2, 3)

If one or more devices represented by a classification name is labeled and marketed as "sterile," include the words sterile as part of the common or usual name, i.e. "Various Types of Sterile and Non Sterile Syringes." (Appendix I - Examples 2, 6)

(12) Applicable Performance Standard

If any device identified by the classification name is the subject of any performance standard established pursuant to Section 514 of the Federal Food, Drug, and Cosmetic Act or Section 348 of the Radiation Control for Health and Safety Act, check "YES" and complete Block 12a. If not, check "NO" and proceed to Block 13.

(12a) If "YES" has been checked in Block 12, enter the name of the standard and the applicable section and paragraph of Title 21 of the Code of Federal Regulations. Use supplemental sheets if necessary to report more than one performance standard for a classification name. (Appendix I - Example 5)

(13) Approved Premarket Approval Applications

If any device identified by a classification name has been the subject of a premarket approval application pursuant to Sections 505(NDA), 507(Antibiotic Forms 5 or 6) or 515 (Premarket Approval Application or Product Development Protocol) of the Federal Food, Drug, and Cosmetic Act, check "YES" and complete Block 13a. If not, check "NO" and proceed to Block 14.

(13a) If "YES" has been checked in Block 13, identify the approved application by entering its assigned FDA number. If more than one number has been assigned, report such numbers on a supplemental sheet. (Appendix I - Example 4)

(14) Distribution Status

If the device, as labeled, is intended for distribution to and used by the general public, check "YES". If not, check "NO".

INTRODUCTION TO BLOCKS 15, 16, and 17

Blocks 15, 16, and 17 are to be used to identify establishments within the owner/operator's organization that are engaged in processing the device. Do not include such facilities as contract sterilizers, contract packagers, etc.

Initial distributors should not be identified in this section unless the initial distributor is listing in behalf of a foreign owner/operator.

(15) Establishment Registration Number

Enter in Block 15 the registration number (Located in Block 1 of Form FD-2891 - "Initial Registration of Medical Device Establishment" or in the upper right corner of Form FD-2891(a), "Annual Registration of Device Establishment"). If the establishment is not registered, enter "NR" in this block. Foreign owner/operators not having a registration number should enter "NONE" in this block. (Appendix I - Example 13)

(16) Establishment Name

Enter in Block 16 the name of the establishment. For registered establishments the name should be identical to the name provided on Form FD-2891 or FD-2891(a).

(17) Establishment Type

Enter in Block 17 the appropriate letter code or codes from the list below that describe the activities that occur at the establishment.

Letter	Activity
D	Specification Developer
F	Foreign Owner/Operator
I	Initial Distributor listing on behalf of foreign owner/operator
M	Domestic Owner/Operator
P	Manufactures devices to own specifications and labels them for other owner/operators who act as Private Label Distributors
R	Repackager or Relabeler

Examples:

(a) If an establishment site is involved only in the development of specifications, enter "D" in the D column for that establishment.

(b) If an establishment site manufactures and labels a device with its company name(s) only, enter "M" in the M column for that establishment.

(c) If an establishment site manufactures a device and labels it for a different owner/operator, enter "M" and "P" in the appropriate columns.

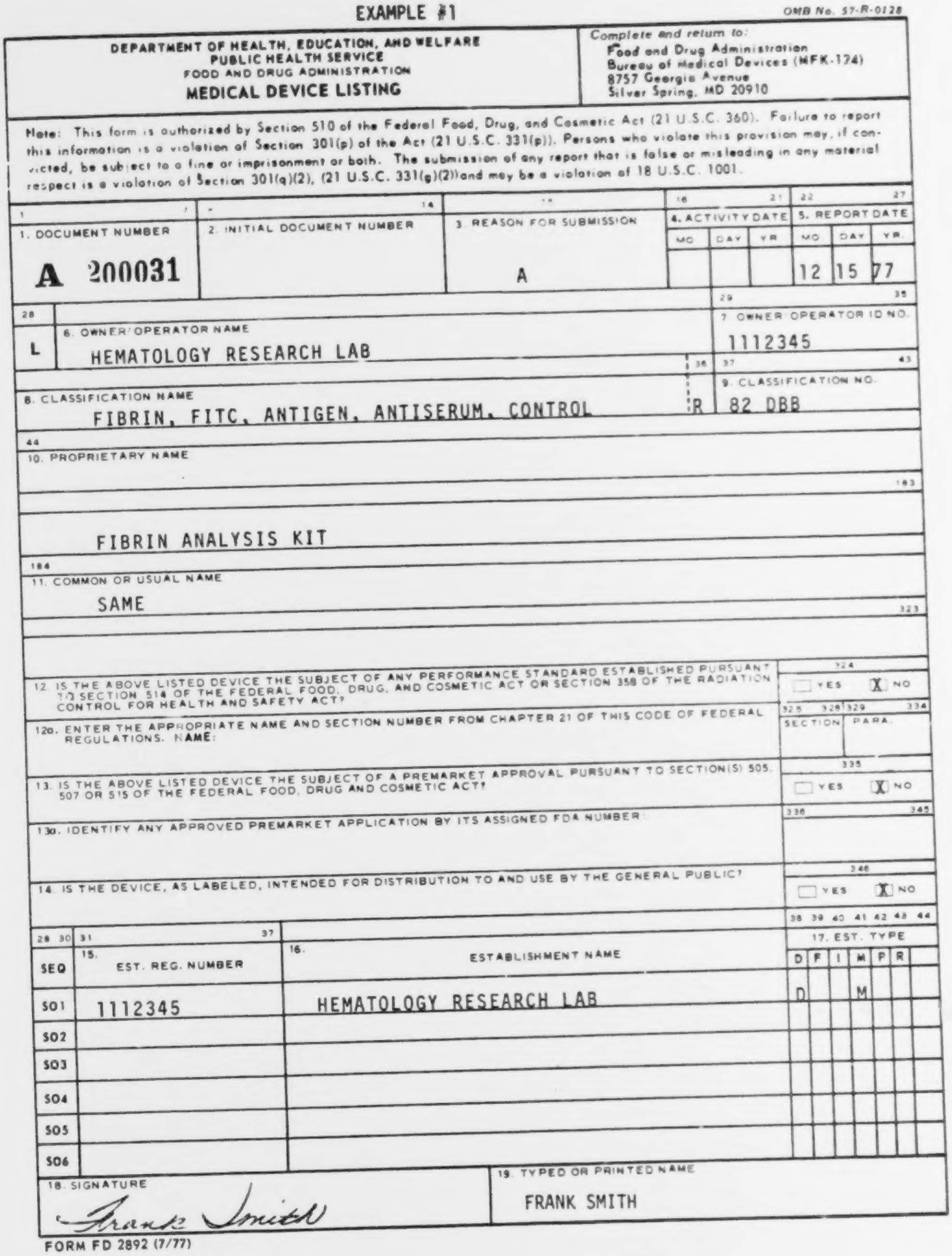
(18) Signature

The person completing Form FD-2892 must sign in the space provided.

(19) Name

Type or print the name of the individual who signed Block 18.

EXAMPLE #1



OMB No. 57-R-0128

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION
MEDICAL DEVICE LISTING

Complete and return to:
Food and Drug Administration
Bureau of Medical Devices (HFK-124)
8757 Georgia Avenue
Silver Spring, MD 20910

Note: This form is authorized by Section 510 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 360). Failure to report this information is a violation of Section 301(p) of the Act (21 U.S.C. 331(p)). Persons who violate this provision may, if convicted, be subject to a fine or imprisonment or both. The submission of any report that is false or misleading in any material respect is a violation of Section 301(q)(2), (21 U.S.C. 331(g)(2)) and may be a violation of 18 U.S.C. 1001.

1. DOCUMENT NUMBER	2. INITIAL DOCUMENT NUMBER	3. REASON FOR SUBMISSION	4. ACTIVITY DATE MO DAY YR	5. REPORT DATE MO DAY YR
A 200031		A		12 15 77

L — 6. OWNER/OPERATOR NAME: HEMATOLOGY RESEARCH LAB

7. OWNER/OPERATOR ID NO.: 1112345

8. CLASSIFICATION NAME: FIBRIN, FITC, ANTIGEN, ANTISERUM, CONTROL

36: R

9. CLASSIFICATION NO.: 82 DBB

10. PROPRIETARY NAME: FIBRIN ANALYSIS KIT

11. COMMON OR USUAL NAME: SAME

12. IS THE ABOVE LISTED DEVICE THE SUBJECT OF ANY PERFORMANCE STANDARD ESTABLISHED PURSUANT TO SECTION 514 OF THE FEDERAL FOOD, DRUG, AND COSMETIC ACT OR SECTION 358 OF THE RADIATION CONTROL FOR HEALTH AND SAFETY ACT? ☐ YES ☒ NO

12a. ENTER THE APPROPRIATE NAME AND SECTION NUMBER FROM CHAPTER 21 OF THIS CODE OF FEDERAL REGULATIONS. NAME: SECTION PARA.

13. IS THE ABOVE LISTED DEVICE THE SUBJECT OF A PREMARKET APPROVAL PURSUANT TO SECTION(S) 505, 507 OR 515 OF THE FEDERAL FOOD, DRUG AND COSMETIC ACT? ☐ YES ☒ NO

13a. IDENTIFY ANY APPROVED PREMARKET APPLICATION BY ITS ASSIGNED FDA NUMBER:

14. IS THE DEVICE, AS LABELED, INTENDED FOR DISTRIBUTION TO AND USE BY THE GENERAL PUBLIC? ☐ YES ☒ NO

SEQ	15. EST. REG. NUMBER	16. ESTABLISHMENT NAME	17. EST. TYPE D	F	I	M	P	R
S01	1112345	HEMATOLOGY RESEARCH LAB	D			M		
S02								
S03								
S04								
S05								
S06								

18. SIGNATURE: Frank Smith

19. TYPED OR PRINTED NAME: FRANK SMITH

FORM FD 2892 (7/77)

LISTING A DEVICE WITH ONLY ONE CLASSIFICATION NAME SELECTED FROM THE LIST. ENTER THE CLASSIFICATION NAME IN BLOCK 8. ENTER THE LETTER "R" IN FIELD 36 IF INDIVIDUAL REAGENTS IN THE KIT ARE ALSO MARKETED SEPARATELY. ENTER CLASSIFICATION NUMBER IN BLOCK 9.

NOTE: EVEN IF OWNER/OPERATOR MARKETED ONLY THE ANTISERUM, THE CLASSIFICATION NAME FIBRIN, FITC, ANTIGEN, ANTISERUM, CONTROL WOULD STILL BE SELECTED.

EXAMPLE #2

OMB No. 57-R-0128

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION
MEDICAL DEVICE LISTING

Complete and return to:
Food and Drug Administration
Bureau of Medical Devices (HFK-124)
8757 Georgia Avenue
Silver Spring, MD 20910

Note: This form is authorized by Section 510 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 360). Failure to report this information is a violation of Section 301(p) of the Act (21 U.S.C. 331(p)). Persons who violate this provision may, if convicted, be subject to a fine or imprisonment or both. The submission of any report that is false or misleading in any material respect is a violation of Section 301(q)(2), (21 U.S.C. 331(g)(2))and may be a violation of 18 U.S.C. 1001.

1. DOCUMENT NUMBER: A 200021
2. INITIAL DOCUMENT NUMBER:
3. REASON FOR SUBMISSION: A
4. ACTIVITY DATE: MO DAY YR
5. REPORT DATE: MO 12 DAY 01 YR 77

L
6. OWNER/OPERATOR NAME: DOCTOR'S BEST DEVICES
7. OWNER/OPERATOR ID NO.: 9831001

8. CLASSIFICATION NAME: SYRINGE, PISTON
9. CLASSIFICATION NO.: 80 FMF

10. PROPRIETARY NAME: MULTIPLE

11. COMMON OR USUAL NAME: VARIOUS SIZES OF STERILE AND NON-STERILE SYRINGES

12. IS THE ABOVE LISTED DEVICE THE SUBJECT OF ANY PERFORMANCE STANDARD ESTABLISHED PURSUANT TO SECTION 514 OF THE FEDERAL FOOD, DRUG, AND COSMETIC ACT OR SECTION 358 OF THE RADIATION CONTROL FOR HEALTH AND SAFETY ACT? ☐ YES ☒ NO

12a. ENTER THE APPROPRIATE NAME AND SECTION NUMBER FROM CHAPTER 21 OF THIS CODE OF FEDERAL REGULATIONS. **NAME:** SECTION PARA.

13. IS THE ABOVE LISTED DEVICE THE SUBJECT OF A PREMARKET APPROVAL PURSUANT TO SECTION(S) 505, 507 OR 515 OF THE FEDERAL FOOD, DRUG AND COSMETIC ACT? ☐ YES ☒ NO

13a. IDENTIFY ANY APPROVED PREMARKET APPLICATION BY ITS ASSIGNED FDA NUMBER:

14. IS THE DEVICE, AS LABELED, INTENDED FOR DISTRIBUTION TO AND USE BY THE GENERAL PUBLIC? ☐ YES ☒ NO

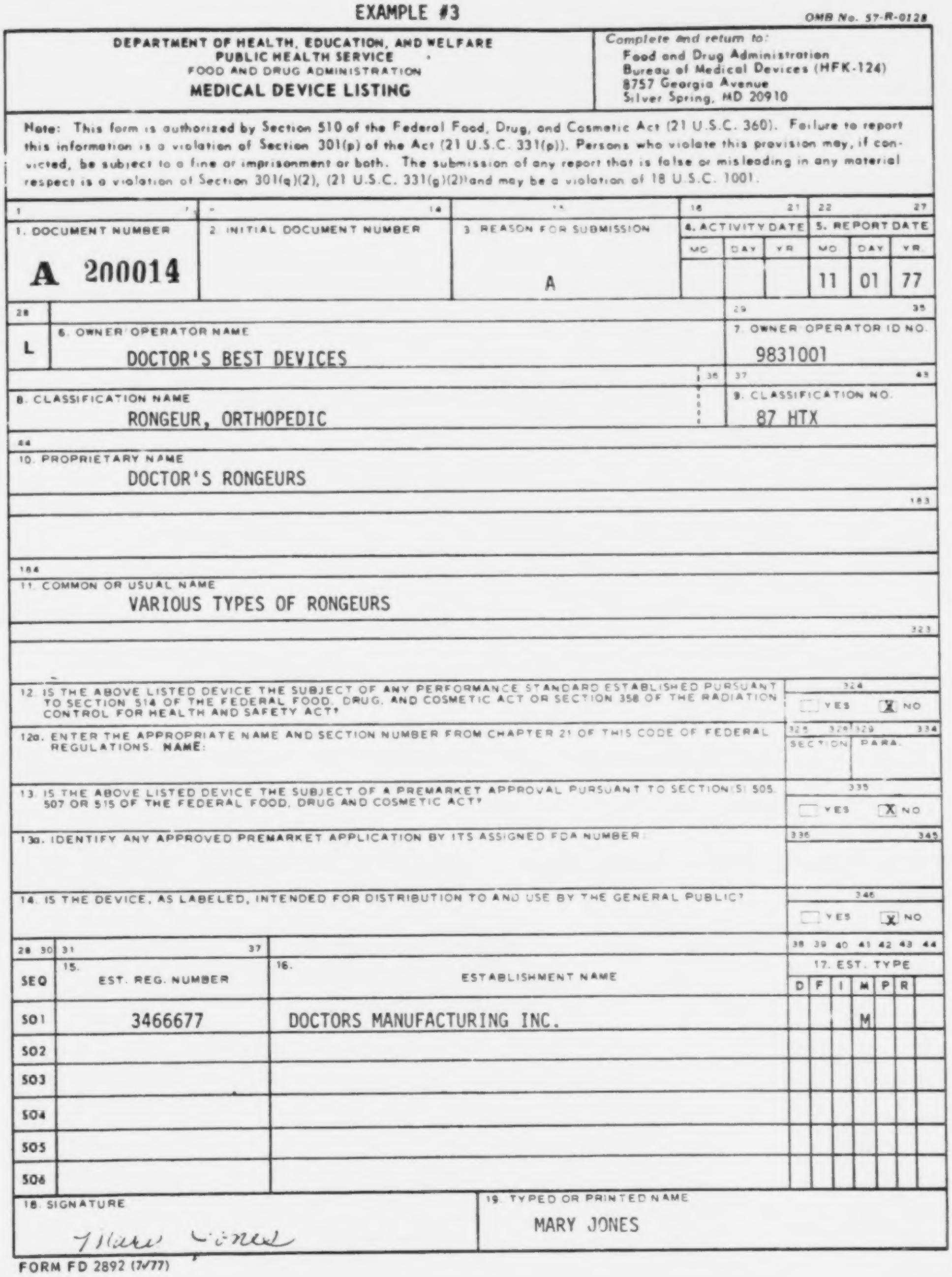
SEQ	15. EST. REG. NUMBER	16. ESTABLISHMENT NAME	17. EST. TYPE D	F	I	M	P	R	
501	3112211	BEST DEVICES, INC.						R	
502									
503									
504									
505									
506									

18. SIGNATURE: Mary Jones
19. TYPED OR PRINTED NAME: MARY JONES

FORM FD 2892 (7/77)

LISTING VARIOUS DEVICES UNDER A SINGLE CLASSIFICATION NAME. IF APPROPRIATE, ENTER THE WORD "MULTIPLE" IN BLOCK 10 FOR DEVICES WITH MORE THAN ONE PROPRIETARY NAME. NOTE REFERENCE TO "STERILE" IN BLOCK 11.

EXAMPLE #3



OMB No. 57-R-0128

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION
MEDICAL DEVICE LISTING

Complete and return to:
Food and Drug Administration
Bureau of Medical Devices (HFK-124)
8757 Georgia Avenue
Silver Spring, MD 20910

Note: This form is authorized by Section 510 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 360). Failure to report this information is a violation of Section 301(p) of the Act (21 U.S.C. 331(p)). Persons who violate this provision may, if convicted, be subject to a fine or imprisonment or both. The submission of any report that is false or misleading in any material respect is a violation of Section 301(q)(2), (21 U.S.C. 331(g)(2)) and may be a violation of 18 U.S.C. 1001.

1. DOCUMENT NUMBER: A 200014
2. INITIAL DOCUMENT NUMBER:
3. REASON FOR SUBMISSION: A
4. ACTIVITY DATE: MO DAY YR
5. REPORT DATE: MO 11 DAY 01 YR 77

L
6. OWNER/OPERATOR NAME: DOCTOR'S BEST DEVICES
7. OWNER/OPERATOR ID NO.: 9831001
8. CLASSIFICATION NAME: RONGEUR, ORTHOPEDIC
9. CLASSIFICATION NO.: 87 HTX
10. PROPRIETARY NAME: DOCTOR'S RONGEURS
11. COMMON OR USUAL NAME: VARIOUS TYPES OF RONGEURS

12. IS THE ABOVE LISTED DEVICE THE SUBJECT OF ANY PERFORMANCE STANDARD ESTABLISHED PURSUANT TO SECTION 514 OF THE FEDERAL FOOD, DRUG, AND COSMETIC ACT OR SECTION 358 OF THE RADIATION CONTROL FOR HEALTH AND SAFETY ACT? ☐ YES ☒ NO

12a. ENTER THE APPROPRIATE NAME AND SECTION NUMBER FROM CHAPTER 21 OF THIS CODE OF FEDERAL REGULATIONS. **NAME:** SECTION PARA.

13. IS THE ABOVE LISTED DEVICE THE SUBJECT OF A PREMARKET APPROVAL PURSUANT TO SECTION(S) 505, 507 OR 515 OF THE FEDERAL FOOD, DRUG AND COSMETIC ACT? ☐ YES ☒ NO

13a. IDENTIFY ANY APPROVED PREMARKET APPLICATION BY ITS ASSIGNED FDA NUMBER:

14. IS THE DEVICE, AS LABELED, INTENDED FOR DISTRIBUTION TO AND USE BY THE GENERAL PUBLIC? ☐ YES ☒ NO

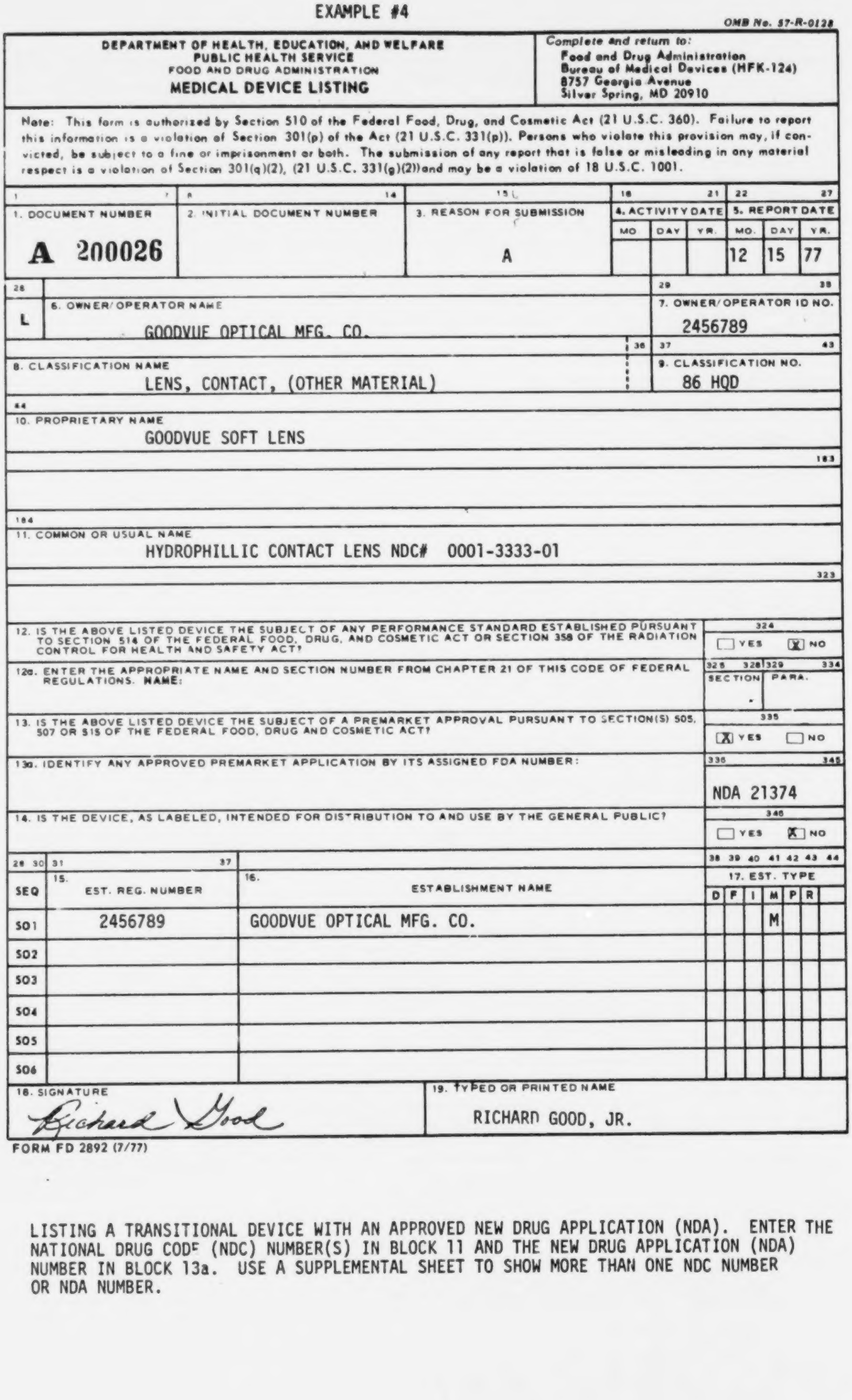
SEQ	15. EST. REG. NUMBER	16. ESTABLISHMENT NAME	17. EST. TYPE D	F	I	M	P	R	
S01	3466677	DOCTORS MANUFACTURING INC.				M			
S02									
S03									
S04									
S05									
S06									

18. SIGNATURE: Mary Jones
19. TYPED OR PRINTED NAME: MARY JONES

FORM FD 2892 (7/77)

LISTING VARIOUS DEVICES APPEARING UNDER A SINGLE CLASSIFICATION NAME.
UPDATES: SEE EXAMPLE 15 FOR DELETING THIS CLASSIFICATION NAME.

EXAMPLE #4



OMB No. 57-R-0128

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION
MEDICAL DEVICE LISTING

Complete and return to:
Food and Drug Administration
Bureau of Medical Devices (HFK-124)
8757 Georgia Avenue
Silver Spring, MD 20910

Note: This form is authorized by Section 510 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 360). Failure to report this information is a violation of Section 301(p) of the Act (21 U.S.C. 331(p)). Persons who violate this provision may, if convicted, be subject to a fine or imprisonment or both. The submission of any report that is false or misleading in any material respect is a violation of Section 301(q)(2), (21 U.S.C. 331(g)(2))and may be a violation of 18 U.S.C. 1001.

1 7	8 14	15	16 21			22 27		
1. DOCUMENT NUMBER	2. INITIAL DOCUMENT NUMBER	3. REASON FOR SUBMISSION	4. ACTIVITY DATE			5. REPORT DATE		
			MO	DAY	YR.	MO.	DAY	YR.
A 200026		A				12	15	77

28		29 35
L	6. OWNER/OPERATOR NAME GOODVUE OPTICAL MFG. CO.	7. OWNER/OPERATOR ID NO. 2456789

36	37 43
8. CLASSIFICATION NAME LENS, CONTACT, (OTHER MATERIAL)	9. CLASSIFICATION NO. 86 HQD

44
10. PROPRIETARY NAME
GOODVUE SOFT LENS
183

184
11. COMMON OR USUAL NAME
HYDROPHILLIC CONTACT LENS NDC# 0001-3333-01
323

12. IS THE ABOVE LISTED DEVICE THE SUBJECT OF ANY PERFORMANCE STANDARD ESTABLISHED PURSUANT TO SECTION 514 OF THE FEDERAL FOOD, DRUG, AND COSMETIC ACT OR SECTION 358 OF THE RADIATION CONTROL FOR HEALTH AND SAFETY ACT?	324 ☐ YES ☒ NO
12a. ENTER THE APPROPRIATE NAME AND SECTION NUMBER FROM CHAPTER 21 OF THIS CODE OF FEDERAL REGULATIONS. **NAME:**	325 328 329 334 SECTION PARA.
13. IS THE ABOVE LISTED DEVICE THE SUBJECT OF A PREMARKET APPROVAL PURSUANT TO SECTION(S) 505, 507 OR 515 OF THE FEDERAL FOOD, DRUG AND COSMETIC ACT?	335 ☒ YES ☐ NO
13a. IDENTIFY ANY APPROVED PREMARKET APPLICATION BY ITS ASSIGNED FDA NUMBER:	336 345 NDA 21374
14. IS THE DEVICE, AS LABELED, INTENDED FOR DISTRIBUTION TO AND USE BY THE GENERAL PUBLIC?	346 ☐ YES ☒ NO

28 30	31 37		38	39	40	41	42	43	44
			17. EST. TYPE						
SEQ	15. EST. REG. NUMBER	16. ESTABLISHMENT NAME	D	F	I	M	P	R	
S01	2456789	GOODVUE OPTICAL MFG. CO.				M			
S02									
S03									
S04									
S05									
S06									

18. SIGNATURE Richard Good	19. TYPED OR PRINTED NAME RICHARD GOOD, JR.

FORM FD 2892 (7/77)

LISTING A TRANSITIONAL DEVICE WITH AN APPROVED NEW DRUG APPLICATION (NDA). ENTER THE NATIONAL DRUG CODE (NDC) NUMBER(S) IN BLOCK 11 AND THE NEW DRUG APPLICATION (NDA) NUMBER IN BLOCK 13a. USE A SUPPLEMENTAL SHEET TO SHOW MORE THAN ONE NDC NUMBER OR NDA NUMBER.

EXAMPLE #5

OMB No. 57-R-0128

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION
MEDICAL DEVICE LISTING

Complete and return to:
Food and Drug Administration
Bureau of Medical Devices (HFK-124)
8757 Georgia Avenue
Silver Spring, MD 20910

Note: This form is authorized by Section 510 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 360). Failure to report this information is a violation of Section 301(p) of the Act (21 U.S.C. 331(p)). Persons who violate this provision may, if convicted, be subject to a fine or imprisonment or both. The submission of any report that is false or misleading in any material respect is a violation of Section 301(q)(2), (21 U.S.C. 331(g)(2)) and may be a violation of 18 U.S.C. 1001.

1 - 7	8 - 14	15	16 - 21			22 - 27		
1. DOCUMENT NUMBER	2. INITIAL DOCUMENT NUMBER	3. REASON FOR SUBMISSION	4. ACTIVITY DATE			5. REPORT DATE		
			MO	DAY	YR	MO.	DAY	YR.
A 200024		A				12	31	77

28 — L
6. OWNER/OPERATOR NAME: DOCTOR'S BEST DEVICES

29 – 35
7. OWNER/OPERATOR ID NO.: 9831001

8. CLASSIFICATION NAME: SYSTEM, TOMOGRAPHIC, RADIOGRAPHIC

36 — R

37 – 43
9. CLASSIFICATION NO.: 90 IZF

44 – 183
10. PROPRIETARY NAME: DOCTOR'S X-RAY UNIT

184 – 323
11. COMMON OR USUAL NAME: VARIOUS MODELS OF X-RAY UNITS

12. IS THE ABOVE LISTED DEVICE THE SUBJECT OF ANY PERFORMANCE STANDARD ESTABLISHED PURSUANT TO SECTION 514 OF THE FEDERAL FOOD, DRUG, AND COSMETIC ACT OR SECTION 358 OF THE RADIATION CONTROL FOR HEALTH AND SAFETY ACT?
324 — ☒ YES ☐ NO

12a. ENTER THE APPROPRIATE NAME AND SECTION NUMBER FROM CHAPTER 21 OF THIS CODE OF FEDERAL REGULATIONS. **NAME:** DIAGNOSTIC X-RAY SYSTEMS AND THEIR MAJOR COMPONENTS
325 – 328 SECTION: 1020
329 – 334 PARA.: 30, 31

13. IS THE ABOVE LISTED DEVICE THE SUBJECT OF A PREMARKET APPROVAL PURSUANT TO SECTION(S) 505, 507 OR 515 OF THE FEDERAL FOOD, DRUG AND COSMETIC ACT?
335 — ☐ YES ☒ NO

13a. IDENTIFY ANY APPROVED PREMARKET APPLICATION BY ITS ASSIGNED FDA NUMBER:
336 – 345

14. IS THE DEVICE, AS LABELED, INTENDED FOR DISTRIBUTION TO AND USE BY THE GENERAL PUBLIC?
346 — ☐ YES ☒ NO

28 30	31 – 37		38	39	40	41	42	43	44
	15.	16.	17. EST. TYPE						
SEQ	EST. REG. NUMBER	ESTABLISHMENT NAME	D	F	I	M	P	R	
S01	3466677	DOCTOR'S MFG. INC.				M			
S02									
S03									
S04									
S05									
S06									

18. SIGNATURE: Mary Jones

19. TYPED OR PRINTED NAME: MARY JONES

FORM FD 2892 (7/77)

LISTING A DEVICE WHOSE NAME IS ON THE CLASSIFICATION LIST. ENTER THE CLASSIFICATION NAME IN BLOCK 8. ENTER THE LETTER "R" IN FIELD 36 IF UNCLASSIFIED COMPONENTS, PARTS, AND ACCESSORIES ARE MARKETED SEPARATELY FOR THIS DEVICE. IF IN ADDITION, CLASSIFIED COMPONENTS, PARTS, AND ACCESSORIES ARE ALSO MARKETED, INCLUDE THEIR CLASSIFICATION NAMES AND NUMBERS ON A SUPPLEMENTAL SHEET UNDER THE HEADING "RELATED ITEMS." (SEE EXAMPLE 7A). SINCE THE DEVICE IS SUBJECT TO STANDARD, COMPLETE BLOCKS 12 AND 12A.

EXAMPLE #6

OMB No. 57-R-0128

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION
MEDICAL DEVICE LISTING

Complete and return to:
Food and Drug Administration
Bureau of Medical Devices (HFK-124)
8757 Georgia Avenue
Silver Spring, MD 20910

Note: This form is authorized by Section 510 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 360). Failure to report this information is a violation of Section 301(p) of the Act (21 U.S.C. 331(p)). Persons who violate this provision may, if convicted, be subject to a fine or imprisonment or both. The submission of any report that is false or misleading in any material respect is a violation of Section 301(q)(2), (21 U.S.C. 331(g)(2)) and may be a violation of 18 U.S.C. 1001.

1	14	15	16		21	22		27
1. DOCUMENT NUMBER	2. INITIAL DOCUMENT NUMBER	3. REASON FOR SUBMISSION	4. ACTIVITY DATE			5. REPORT DATE		
			MO	DAY	YR	MO	DAY	YR.
A 200015		A				12	15	77

28		29 35
L	6. OWNER/OPERATOR NAME ABC PLASTICS CO.	7. OWNER/OPERATOR ID NO. 9824123

36	37 43
8. CLASSIFICATION NAME MULTIPLE	9. CLASSIFICATION NO.

44
10. PROPRIETARY NAME
ABC STYLETTE
103

104
11. COMMON OR USUAL NAME
VARIOUS SIZES OF STERILE AND NON-STERILE STYLETS
323

12. IS THE ABOVE LISTED DEVICE THE SUBJECT OF ANY PERFORMANCE STANDARD ESTABLISHED PURSUANT TO SECTION 514 OF THE FEDERAL FOOD, DRUG, AND COSMETIC ACT OR SECTION 358 OF THE RADIATION CONTROL FOR HEALTH AND SAFETY ACT? 324 ☐ YES ☒ NO

12a. ENTER THE APPROPRIATE NAME AND SECTION NUMBER FROM CHAPTER 21 OF THIS CODE OF FEDERAL REGULATIONS. NAME: 325 328 SECTION 329 334 PARA.

13. IS THE ABOVE LISTED DEVICE THE SUBJECT OF A PREMARKET APPROVAL PURSUANT TO SECTION(S) 505, 507 OR 515 OF THE FEDERAL FOOD, DRUG AND COSMETIC ACT? 335 ☐ YES ☒ NO

13a. IDENTIFY ANY APPROVED PREMARKET APPLICATION BY ITS ASSIGNED FDA NUMBER: 336 345

14. IS THE DEVICE, AS LABELED, INTENDED FOR DISTRIBUTION TO AND USE BY THE GENERAL PUBLIC? 346 ☐ YES ☒ NO

28 30	31 37		38	39	40	41	42	43	44
	15.	16.	17. EST. TYPE						
SEQ	EST. REG. NUMBER	ESTABLISHMENT NAME	D	F	I	M	P	R	
501	1212345	ABC PLASTICS CO.				M			
502	2212345	ABC PLASTICS CO.				M	P		
503	2012345	ABC PLASTICS CO.	D						
504									
505									
506									

18. SIGNATURE Paula Richards	19. TYPED OR PRINTED NAME PAULA RICHARDS

FORM FD 2892 (7/77)

LISTING A DEVICE WITH MULTIPLE CLASSIFICATION NAMES, ALL OF WHICH ARE ON THE LIST. SHOW THE CLASSIFICATION NAMES AND NUMBERS ON A SUPPLEMENTAL SHEET (SEE EXAMPLE 6A). ENTER "MULTIPLE" IN BLOCK 8 AND LEAVE BLOCK 9 BLANK. NOTE: MULTIPLE MANUFACTURING SITES INDICATED IN BLOCKS 15, 16, and 17.
UPDATES: SEE EXAMPLE 16 FOR ADDING AND DELETING CLASSIFICATION NAMES.

EXAMPLE #6A

DOC. NO. A 200015

ABC PLASTICS CO.
12 KING STREET
BOSTON, MA 02115

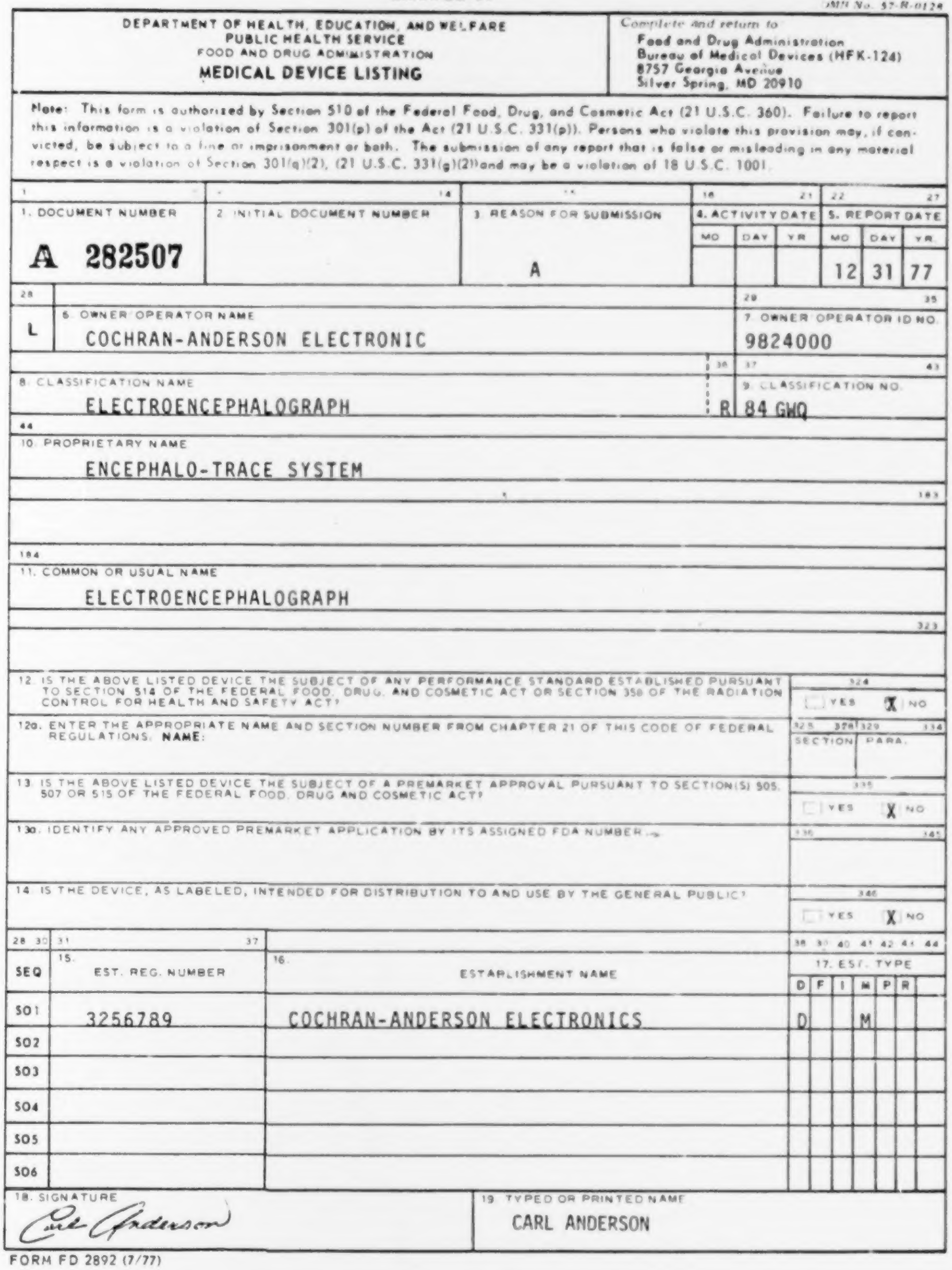
DEVICE NAMES

1.	STYLET, SURGICAL, GENERAL & PLASTIC SURGERY	79 GAH
2.	STYLET, TRACHEAL TUBE	73 BSR
3.	STYLET FOR CATHETER, GASTRO-UROLOGY	78 EZB

NOTE: THE NAME AND ADDRESS OF THE OWNER/OPERATOR SHOULD APPEAR ON TOP OF THE SUPPLEMENTAL SHEET AND THE DOCUMENT NUMBER ON THE UPPER RIGHT HAND CORNER.

ONLY THREE CLASSIFICATION NAMES OUT OF FIVE ON THE CLASSIFICATION LIST ARE SELECTED BECAUSE THIS STYLET IS PROMOTED FOR ONLY THESE THREE PURPOSES.

EXAMPLE #7



OMB No. 57-R-0124

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION
MEDICAL DEVICE LISTING

Complete and return to
Food and Drug Administration
Bureau of Medical Devices (HFK-124)
8757 Georgia Avenue
Silver Spring, MD 20910

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1. DOCUMENT NUMBER: A 282507
2. INITIAL DOCUMENT NUMBER:
3. REASON FOR SUBMISSION: A
4. ACTIVITY DATE: MO DAY YR
5. REPORT DATE: MO 12 DAY 31 YR 77

L

6. OWNER OPERATOR NAME: COCHRAN-ANDERSON ELECTRONIC
7. OWNER OPERATOR ID NO.: 9824000

8. CLASSIFICATION NAME: ELECTROENCEPHALOGRAPH

R

9. CLASSIFICATION NO.: 84 GWQ

10. PROPRIETARY NAME: ENCEPHALO-TRACE SYSTEM

11. COMMON OR USUAL NAME: ELECTROENCEPHALOGRAPH

12. IS THE ABOVE LISTED DEVICE THE SUBJECT OF ANY PERFORMANCE STANDARD ESTABLISHED PURSUANT TO SECTION 514 OF THE FEDERAL FOOD, DRUG, AND COSMETIC ACT OR SECTION 358 OF THE RADIATION CONTROL FOR HEALTH AND SAFETY ACT? ☐ YES ☒ NO

12a. ENTER THE APPROPRIATE NAME AND SECTION NUMBER FROM CHAPTER 21 OF THIS CODE OF FEDERAL REGULATIONS. **NAME:** SECTION PARA.

13. IS THE ABOVE LISTED DEVICE THE SUBJECT OF A PREMARKET APPROVAL PURSUANT TO SECTION(S) 505, 507 OR 515 OF THE FEDERAL FOOD, DRUG AND COSMETIC ACT? ☐ YES ☒ NO

13a. IDENTIFY ANY APPROVED PREMARKET APPLICATION BY ITS ASSIGNED FDA NUMBER →

14. IS THE DEVICE, AS LABELED, INTENDED FOR DISTRIBUTION TO AND USE BY THE GENERAL PUBLIC? ☐ YES ☒ NO

SEQ	15. EST. REG. NUMBER	16. ESTABLISHMENT NAME	17. EST. TYPE D	F	I	M	P	R
501	3256789	COCHRAN-ANDERSON ELECTRONICS	D			M		
502								
503								
504								
505								
506								

18. SIGNATURE: Carl Anderson
19. TYPED OR PRINTED NAME: CARL ANDERSON

FORM FD 2892 (7/77)

LISTING A DEVICE WHOSE NAME IS ON THE CLASSIFICATION LIST. ENTER THE CLASSIFICATION NAME IN BLOCK 8. ENTER THE LETTER "R" IN FIELD 36 IF UNCLASSIFIED COMPONENTS, PARTS, AND ACCESSORIES ARE ALSO MARKETED FOR THIS DEVICE. IF IN ADDITION, CLASSIFIED COMPONENTS, PARTS, AND ACCESSORIES ARE ALSO MARKETED, ENTER THEIR CLASSIFICATION NAMES AND NUMBERS ON A SUPPLEMENTAL SHEET UNDER THE HEADING "RELATED ITEMS". (SEE EXAMPLE 7A)

NO LABELING OR OTHER INFORMATION NEED TO BE SUBMITTED WITH THIS FORM.

EXAMPLE #7A

DOC. NO. A 282507

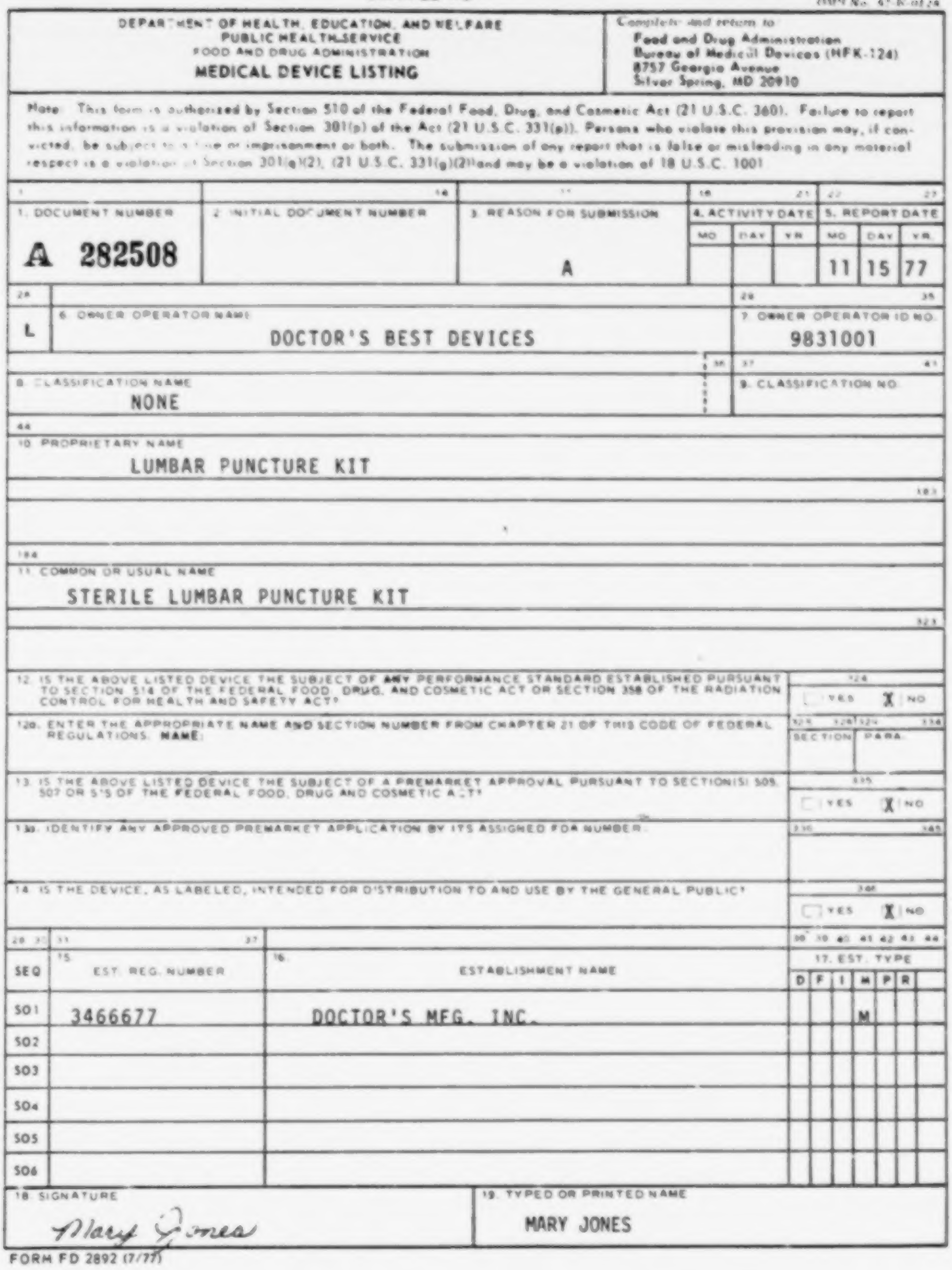
COCHRAN-ANDERSON ELECTRONIC
1394 INDUSTRIAL PARK
CHICAGO, IL. 60638

RELATED ITEMS

CLASSIFICATION NAME	CLASSIFICATION NUMBER
1. GEL, ELECTRODE	89 IKC
2. ELECTRODE, NEEDLE	84 GXZ

NOTE: DOCUMENT NUMBER ON UPPER RIGHT HAND CORNER. UNCLASSIFIED COMPONENTS, PARTS, AND ACCESSORIES MARKETED BY THE OWNER/OPERATOR IS REPRESENTED BY ENTERING THE LETTER 'R' IN FIELD 36 ON FORM FD-2892

EXAMPLE #8



OMB No. [illegible]

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION
MEDICAL DEVICE LISTING

Complete and return to:
Food and Drug Administration
Bureau of Medical Devices (HFK-124)
8757 Georgia Avenue
Silver Spring, MD 20910

Note: This form is authorized by Section 510 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 360). Failure to report this information is a violation of Section 301(p) of the Act (21 U.S.C. 331(p)). Persons who violate this provision may, if convicted, be subject to a fine or imprisonment or both. The submission of any report that is false or misleading in any material respect is a violation of Section 301(q)(2), (21 U.S.C. 331(q)(2)) and may be a violation of 18 U.S.C. 1001

1. DOCUMENT NUMBER: A 282508
2. INITIAL DOCUMENT NUMBER:
3. REASON FOR SUBMISSION: A
4. ACTIVITY DATE: MO DAY YR
5. REPORT DATE: MO 11 DAY 15 YR. 77

L

6. OWNER OPERATOR NAME: DOCTOR'S BEST DEVICES
7. OWNER OPERATOR ID NO.: 9831001
8. CLASSIFICATION NAME: NONE
9. CLASSIFICATION NO.:
10. PROPRIETARY NAME: LUMBAR PUNCTURE KIT
11. COMMON OR USUAL NAME: STERILE LUMBAR PUNCTURE KIT

12. IS THE ABOVE LISTED DEVICE THE SUBJECT OF ANY PERFORMANCE STANDARD ESTABLISHED PURSUANT TO SECTION 514 OF THE FEDERAL FOOD, DRUG, AND COSMETIC ACT OR SECTION 358 OF THE RADIATION CONTROL FOR HEALTH AND SAFETY ACT? ☐ YES ☒ NO

12a. ENTER THE APPROPRIATE NAME AND SECTION NUMBER FROM CHAPTER 21 OF THIS CODE OF FEDERAL REGULATIONS. NAME: SECTION PARA.

13. IS THE ABOVE LISTED DEVICE THE SUBJECT OF A PREMARKET APPROVAL PURSUANT TO SECTION(S) 505, 507 OR 515 OF THE FEDERAL FOOD, DRUG AND COSMETIC ACT? ☐ YES ☒ NO

13a. IDENTIFY ANY APPROVED PREMARKET APPLICATION BY ITS ASSIGNED FDA NUMBER:

14. IS THE DEVICE, AS LABELED, INTENDED FOR DISTRIBUTION TO AND USE BY THE GENERAL PUBLIC? ☐ YES ☒ NO

SEQ	15. EST. REG. NUMBER	16. ESTABLISHMENT NAME	17. EST. TYPE D	F	I	M	P	R	
501	3466677	DOCTOR'S MFG. INC.				M			
502									
503									
504									
505									
506									

18. SIGNATURE: Mary Jones
19. TYPED OR PRINTED NAME: MARY JONES

FORM FD 2892 (7/77)

LISTING A MULTICOMPONENT DEVICE (KIT) NOT ON THE CLASSIFICATION LIST. ENTER "NONE" IN BLOCK 8 AND LEAVE BLOCK 9 BLANK. ATTACH MINIMUM LABELING OR OTHER INFORMATION THAT IS ADEQUATE TO DESCRIBE THE CONTENTS AND THE INTENDED USE OF THE DEVICE.

NOTE: DO NOT ASSIGN CLASSIFICATION NAMES AND NUMBERS TO EACH COMPONENT IN THE KIT.

EXAMPLE #8A

DOC. NO: A 282508

DOCTOR'S BEST DEVICES
5600 FISHERS LANE
ROCKVILLE, MARYLAND 20852

LIST OF COMPONENTS IN LUMBAR PUNCTURE KIT

1 SPINAL NEEDLE, 32 GAUGE X 3 1/2" WITH STYLET

1 SYRINGE 10 cc

3 SAMPLE VIALS 15ML

1 NEEDLE, SKIN INFILTRATION, 24 GAUGE X 5/8"

1 AMPULE 1% LIDOCAINE HYDROCHLORIDE 2 ML

1 FENESTRATED DRAPE

1 PREPARATION TRAY

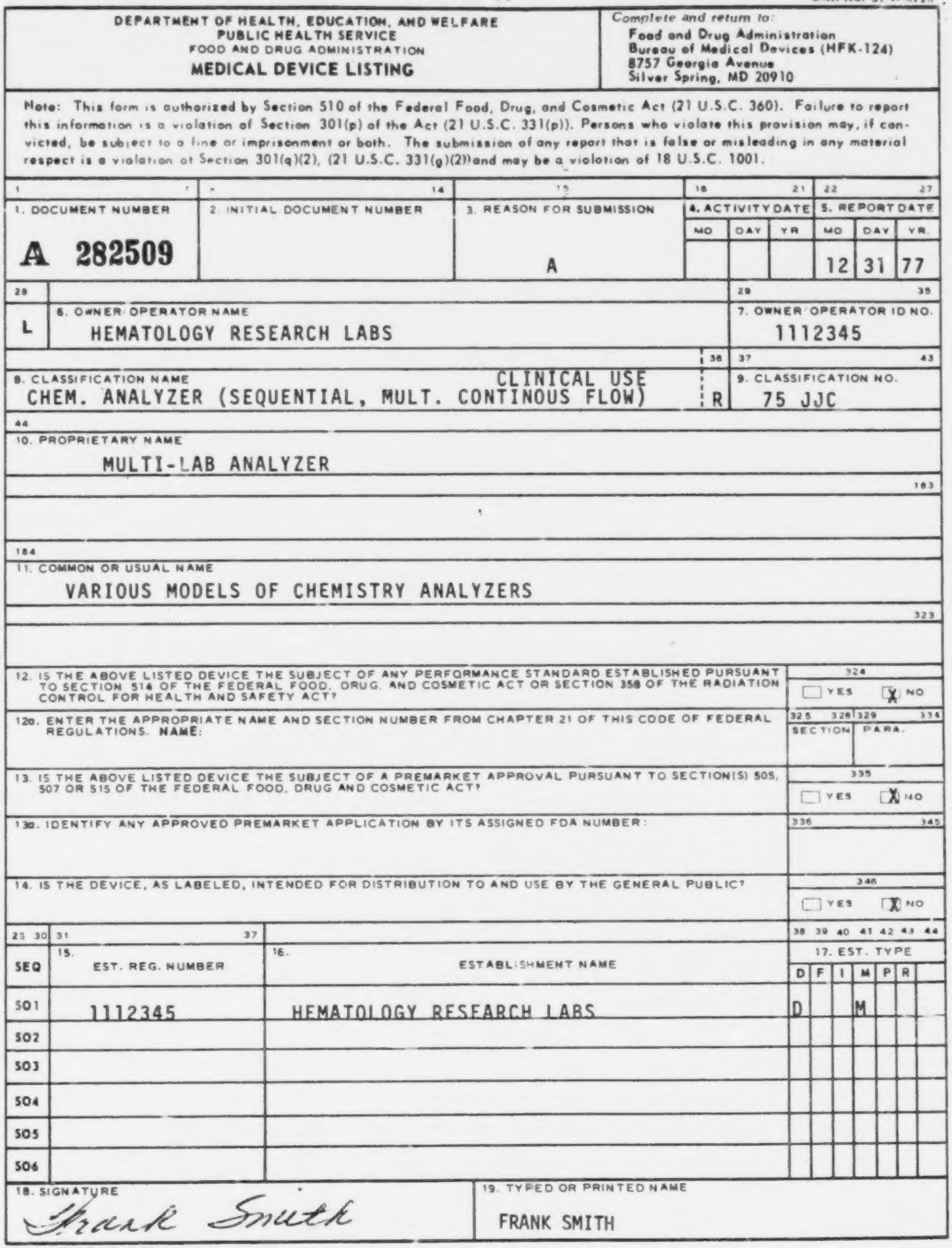
6 GAUZE SPONGES, 3" X 4"

1 ADHESIVE BANDAGE

NOTE: THE NAME AND ADDRESS OF THE OWNER/OPERATOR SHOULD APPEAR ON TOP OF THE SUPPLEMENTAL SHEET AND THE DOCUMENT NUMBER ON THE UPPER RIGHT HAND CORNER

IF APPROPRIATE, LABELS OR LABELING ADEQUATE TO DESCRIBE THE INTENDED USE OF THE DEVICE AND ITS COMPONENTS COULD BE SUBMITTED IN LIEU OF A TYPED SUPPLEMENTAL SHEET.

EXAMPLE #9



OMB No. 57-R-0126

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION
MEDICAL DEVICE LISTING

Complete and return to:
Food and Drug Administration
Bureau of Medical Devices (HFK-124)
8757 Georgia Avenue
Silver Spring, MD 20910

Note: This form is authorized by Section 510 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 360). Failure to report this information is a violation of Section 301(p) of the Act (21 U.S.C. 331(p)). Persons who violate this provision may, if convicted, be subject to a fine or imprisonment or both. The submission of any report that is false or misleading in any material respect is a violation of Section 301(q)(2), (21 U.S.C. 331(g)(2))and may be a violation of 18 U.S.C. 1001.

1. DOCUMENT NUMBER	2. INITIAL DOCUMENT NUMBER	3. REASON FOR SUBMISSION	4. ACTIVITY DATE MO	DAY	YR	5. REPORT DATE MO	DAY	YR.
A 282509		A				12	31	77

L 6. OWNER/OPERATOR NAME: HEMATOLOGY RESEARCH LABS

7. OWNER/OPERATOR ID NO.: 1112345

8. CLASSIFICATION NAME: CHEM. ANALYZER (SEQUENTIAL, MULT. CONTINOUS FLOW) CLINICAL USE — R

9. CLASSIFICATION NO.: 75 JJC

10. PROPRIETARY NAME: MULTI-LAB ANALYZER

11. COMMON OR USUAL NAME: VARIOUS MODELS OF CHEMISTRY ANALYZERS

12. IS THE ABOVE LISTED DEVICE THE SUBJECT OF ANY PERFORMANCE STANDARD ESTABLISHED PURSUANT TO SECTION 514 OF THE FEDERAL FOOD, DRUG, AND COSMETIC ACT OR SECTION 358 OF THE RADIATION CONTROL FOR HEALTH AND SAFETY ACT? ☐ YES ☒ NO

12a. ENTER THE APPROPRIATE NAME AND SECTION NUMBER FROM CHAPTER 21 OF THIS CODE OF FEDERAL REGULATIONS. NAME: SECTION PARA.

13. IS THE ABOVE LISTED DEVICE THE SUBJECT OF A PREMARKET APPROVAL PURSUANT TO SECTION(S) 505, 507 OR 515 OF THE FEDERAL FOOD, DRUG AND COSMETIC ACT? ☐ YES ☒ NO

13a. IDENTIFY ANY APPROVED PREMARKET APPLICATION BY ITS ASSIGNED FDA NUMBER:

14. IS THE DEVICE, AS LABELED, INTENDED FOR DISTRIBUTION TO AND USE BY THE GENERAL PUBLIC? ☐ YES ☒ NO

SEQ	15. EST. REG. NUMBER	16. ESTABLISHMENT NAME	17. EST. TYPE D	F	I	M	P	R
501	1112345	HEMATOLOGY RESEARCH LABS	D			M		
502								
503								
504								
505								
506								

18. SIGNATURE: Frank Smith

19. TYPED OR PRINTED NAME: FRANK SMITH

FORM FD 2892 (7/77)

LISTING A MULTIPLE DETERMINATION IN VITRO DIAGNOSTIC INSTRUMENT FOUND ON THE CLASSIFICATION LIST. ENTER THE LETTER "R" IN FIELD 36 IF UNCLASSIFIED COMPONENTS, PARTS, AND ACCESSORIES ARE MARKETED FOR THIS DEVICE. FOR CLASSIFIED COMPONENTS, PARTS, AND ACCESSORIES, INCLUDING SUPPORTING REAGENTS, INCLUDE THEIR CLASSIFICATION NAMES AND NUMBERS ON A SUPPLEMENTAL SHEET UNDER THE HEADING "RELATED ITEMS" (SEE EXAMPLE 9A). IF IN ADDITION, THE OWNER/OPERATOR MARKETS ANY CLASSIFIED OR UNCLASSIFIED COMPONENTS, PARTS, AND ACCESSORIES, INCLUDING SUPPORTING REAGENTS FOR ANOTHER OWNER/OPERATOR'S DEVICE, THEN THE LETTER "B" WOULD BE ENTERED IN FIELD 36 INSTEAD OF THE LETTER "R".

EXAMPLE #9A

DOC. NO. A 282509

HEMATOLOGY RESEARCH LAB
1100 WASH. BLVD.
BALTIMORE, MD 21207

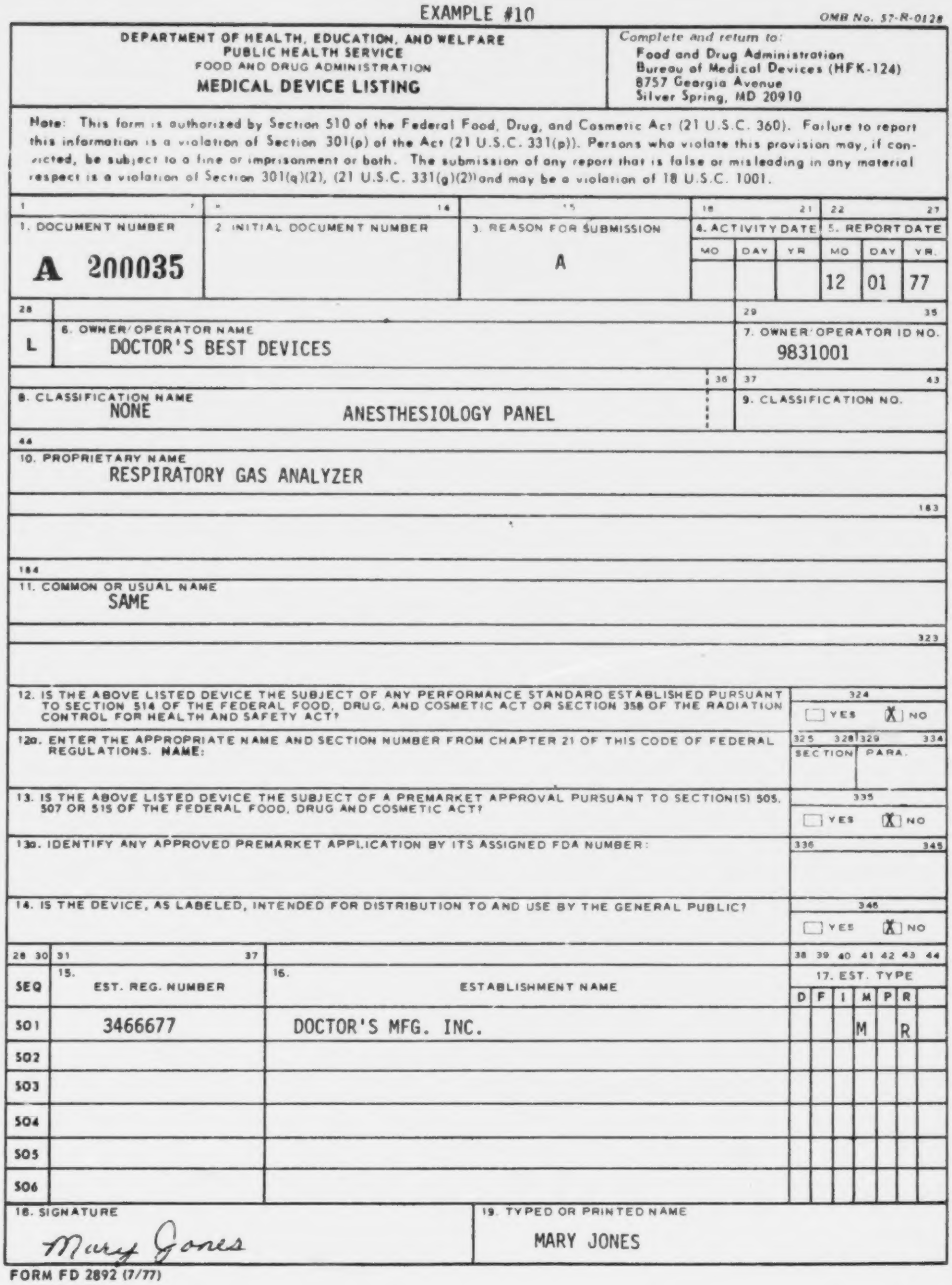
RELATED ITEMS

CLASSIFICATION NAMES	CLASSIFICATION NUMBERS
1. NAD REDUCTION METHOD, LACTATE PYRUVATE, LACTATE DEHYDROGENASE	75 CFJ
2. DIAZO COLORIMETRY, BILIRUBIN	75 CIG
3. LIEBERMAN-BURCHARD, COLORIMETRY, CHOLESTEROL	75 CGO
4. BIURET (COLORIMETRIC), TOTAL PROTEIN	75 CEK
5. DIACETYL-MONOXIME, UREA NITOGEN	75 CDW
*6. SUBSTANCE "X" REAGENT SYSTEM - NOT CLASSIFIED	

LISTING SUPPORTING REAGENT SYSTEMS ON THE CLASSIFICATION LIST.

*NOTE: SINCE NO CLASSIFICATION NAME AND NUMBER COULD BE FOUND FOR THE SUBSTANCE "X" REAGENT SYSTEM, MINIMUM LABELING OR OTHER INFORMATION ADEQUATE TO DESCRIBE THE REAGENT SYSTEM AND IT'S USE SHOULD BE ATTACHED.

DO NOT SUBMIT LABELING OR OTHER INFORMATION FOR UNCLASSIFIED COMPONENTS, PARTS, AND ACCESSORIES FOR THE INSTRUMENT OR FOR ANY OF THE CLASSIFIED REAGENT SYSTEMS.



EXAMPLE #10

OMB No. 57-R-0128

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION
MEDICAL DEVICE LISTING

Complete and return to:
Food and Drug Administration
Bureau of Medical Devices (HFK-124)
8757 Georgia Avenue
Silver Spring, MD 20910

Note: This form is authorized by Section 510 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 360). Failure to report this information is a violation of Section 301(p) of the Act (21 U.S.C. 331(p)). Persons who violate this provision may, if convicted, be subject to a fine or imprisonment or both. The submission of any report that is false or misleading in any material respect is a violation of Section 301(q)(2), (21 U.S.C. 331(g)(2))and may be a violation of 18 U.S.C. 1001.

1. DOCUMENT NUMBER: A 200035
2. INITIAL DOCUMENT NUMBER:
3. REASON FOR SUBMISSION: A
4. ACTIVITY DATE: MO DAY YR
5. REPORT DATE: MO 12 DAY 01 YR. 77

L 6. OWNER/OPERATOR NAME: DOCTOR'S BEST DEVICES
7. OWNER/OPERATOR ID NO.: 9831001

8. CLASSIFICATION NAME: NONE ANESTHESIOLOGY PANEL
9. CLASSIFICATION NO.:

10. PROPRIETARY NAME: RESPIRATORY GAS ANALYZER

11. COMMON OR USUAL NAME: SAME

12. IS THE ABOVE LISTED DEVICE THE SUBJECT OF ANY PERFORMANCE STANDARD ESTABLISHED PURSUANT TO SECTION 514 OF THE FEDERAL FOOD, DRUG, AND COSMETIC ACT OR SECTION 358 OF THE RADIATION CONTROL FOR HEALTH AND SAFETY ACT? ☐ YES ☒ NO

12a. ENTER THE APPROPRIATE NAME AND SECTION NUMBER FROM CHAPTER 21 OF THIS CODE OF FEDERAL REGULATIONS. **NAME:** SECTION PARA.

13. IS THE ABOVE LISTED DEVICE THE SUBJECT OF A PREMARKET APPROVAL PURSUANT TO SECTION(S) 505, 507 OR 515 OF THE FEDERAL FOOD, DRUG AND COSMETIC ACT? ☐ YES ☒ NO

13a. IDENTIFY ANY APPROVED PREMARKET APPLICATION BY ITS ASSIGNED FDA NUMBER:

14. IS THE DEVICE, AS LABELED, INTENDED FOR DISTRIBUTION TO AND USE BY THE GENERAL PUBLIC? ☐ YES ☒ NO

SEQ	15. EST. REG. NUMBER	16. ESTABLISHMENT NAME	17. EST. TYPE D	F	I	M	P	R	
501	3466677	DOCTOR'S MFG. INC.				M		R	
502									
503									
504									
505									
506									

18. SIGNATURE: Mary Jones
19. TYPED OR PRINTED NAME: MARY JONES

FORM FD 2892 (7/77)

LISTING A DEVICE WHOSE NAME IS NOT ON THE CLASSIFICATION LIST. COMPONENTS, PARTS, AND ACCESSORIES ARE ALSO PACKAGED AND MARKETED SEPARATELY. ENTER "NONE" IN BLOCK 8 AND LEAVE BLOCK 9 BLANK. INCLUDE THE CLASSIFICATION NAMES AND NUMBERS OF CLASSIFIED COMPONENTS, PARTS, AND ACCESSORIES ON A SUPPLEMENTAL SHEET UNDER THE HEADING "RELATED ITEMS" (SEE EXAMPLE 10A).

EXAMPLE #10A

DOC. NO. A 200035

DOCTOR'S BEST DEVICES
5600 FISHERS LANE
ROCKVILLE, MD 20852

RELATED ITEMS

FOR RESPIRATORY GAS ANALYZER

CLASSIFICATION NAMES	CLASSIFICATION NUMBERS	
1. CALCULATOR, PULMONARY FUNCTION DATA	73 BCZ	
2. COMPUTER, OXYGEN UPTAKE	73 BZL	
3. COMPUTER, DIAGNOSTIC, PREPROGRAMMED, SINGLE FUNCTION	74 DXG	
4. CALIBRATOR, VOLUME, GAS CALIBRATOR, PRESSURE, GAS	73 BXW 73 BXX ←	NOTE: THESE TWO CLASS. NAMES ARE NEEDED TO DESCRIBE ONE COMPONENT
5. CIRCUIT, BREATHING (W CONNECTOR, ADAPTOR, Y PIECE)	73 CAI ←	NOTE: THIS ONE CLASS. NAME CAN DESCRIBE SEVERAL COMPONENTS.
6. VALVE, NONREBREATHING	73 CBP	
7. MOUTHPIECE, BREATHING	73 BXY	
8. FLOWMETER, CALIBRATION GAS REGULATOR, PRESSURE, GAS CYLINDER	73 BXY ← 73 CAN ←	NOTE: SAME AS NO. 4.

NOTE: IDENTIFY ANY UNCLASSIFIED COMPONENTS, PARTS, OR ACCESSORIES BY INCLUDING APPROPRIATE ANNONTATED CATALOG PAGES. ATTACH MINIMUM LABELING OR OTHER INFORMATION, SUCH AS SPECIFICATION SHEETS, CATALOG DESCRIPTIONS, ETC. ADEQUATE TO DESCRIBE THE RESPIRATORY GAS ANALYZER AND ITS INTENDED USE.

EXAMPLE #11

OMB No. 57-R-0128

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION

MEDICAL DEVICE LISTING

Complete and return to:
Food and Drug Administration
Bureau of Medical Devices (HFK-124)
8757 Georgia Avenue
Silver Spring, MD 20910

Note: This form is authorized by Section 510 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 360). Failure to report this information is a violation of Section 301(p) of the Act (21 U.S.C. 331(p)). Persons who violate this provision may, if convicted, be subject to a fine or imprisonment or both. The submission of any report that is false or misleading in any material respect is a violation of Section 301(q)(2), (21 U.S.C. 331(g)(2))and may be a violation of 18 U.S.C. 1001.

1. DOCUMENT NUMBER	2. INITIAL DOCUMENT NUMBER	3. REASON FOR SUBMISSION	4. ACTIVITY DATE MO	DAY	YR.	5. REPORT DATE MO.	DAY	YR.
A 200016		A				12	09	77

L — 6. OWNER/OPERATOR NAME: LAB CHEM ANALYSIS CO.

7. OWNER/OPERATOR ID NO.: 1115678

8. CLASSIFICATION NAME: CHEMISTRY ANALYZER, MICRO, FOR CLINICAL USE — 36: 0

9. CLASSIFICATION NO.: 75 JJF

10. PROPRIETARY NAME: LAB CHEM X REPLACO

11. COMMON OR USUAL NAME: ACCESSORIES FOR MULTICHANNEL ANALYZER

12. IS THE ABOVE LISTED DEVICE THE SUBJECT OF ANY PERFORMANCE STANDARD ESTABLISHED PURSUANT TO SECTION 514 OF THE FEDERAL FOOD, DRUG, AND COSMETIC ACT OR SECTION 358 OF THE RADIATION CONTROL FOR HEALTH AND SAFETY ACT? ☐ YES ☒ NO

12a. ENTER THE APPROPRIATE NAME AND SECTION NUMBER FROM CHAPTER 21 OF THIS CODE OF FEDERAL REGULATIONS. NAME: — SECTION — PARA.

13. IS THE ABOVE LISTED DEVICE THE SUBJECT OF A PREMARKET APPROVAL PURSUANT TO SECTION(S) 505, 507 OR 515 OF THE FEDERAL FOOD, DRUG AND COSMETIC ACT? ☐ YES ☒ NO

13a. IDENTIFY ANY APPROVED PREMARKET APPLICATION BY ITS ASSIGNED FDA NUMBER:

14. IS THE DEVICE, AS LABELED, INTENDED FOR DISTRIBUTION TO AND USE BY THE GENERAL PUBLIC? ☐ YES ☒ NO

SEQ	15. EST. REG. NUMBER	16. ESTABLISHMENT NAME	17. EST. TYPE D	F	I	M	P	R	
501	1115678	LAB CHEM ANALYSIS CO.				M	P	R	
502									
503									
504									
505									
506									

18. SIGNATURE: Janet Neil

19. TYPED OR PRINTED NAME: JANET NEIL

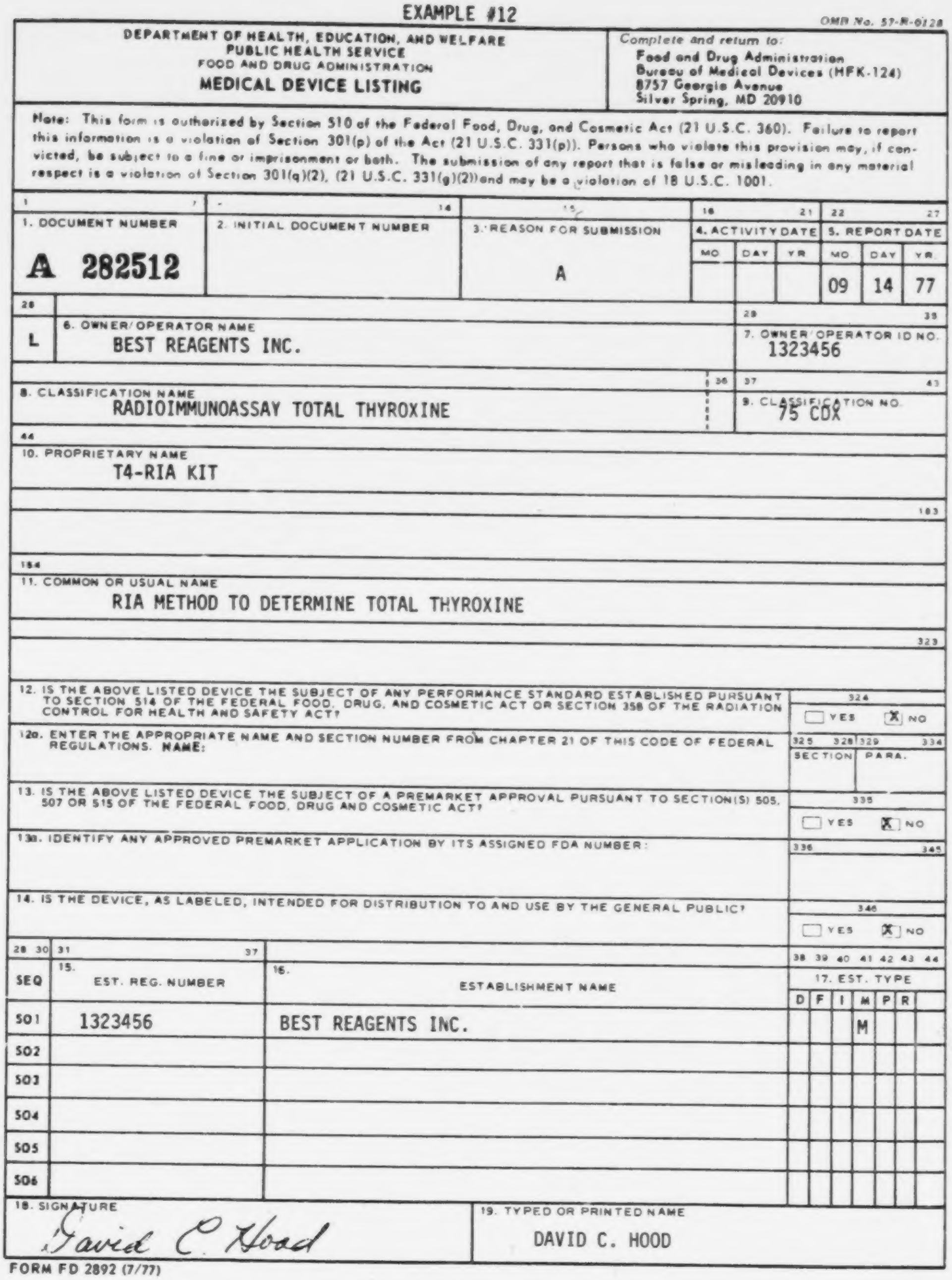
FORM FD 2892 (7/77)

LISTING COMPONENTS, PARTS, AND ACCESSORIES FOR A CLASSIFIED DEVICE MARKETED BY ANOTHER OWNER/OPERATOR. ENTER THE CLASSIFICATION NAME OF THE DEVICE IN BLOCK 8. ENTER THE LETTER "O" IN FIELD 36 TO INDICATE THAT YOU DO NOT MARKET THE DEVICE, BUT RATHER ITS REPLACEMENT COMPONENTS, PARTS, AND ACCESSORIES.

FOR CLASSIFIED COMPONENTS, PARTS, AND ACCESSORIES, INCLUDING SUPPORTING REAGENTS, IDENTIFY THE CLASSIFICATION NAMES AND NUMBERS ON A SUPPLEMENTAL SHEET UNDER THE HEADING "RELATED ITEMS." (SEE EXAMPLE 9A) NOTE: ON THE SUPPLEMENTAL SHEET, USE THE NAME AND ADDRESS OF THE OWNER/OPERATOR APPEARING IN BLOCKS 6 AND 7 OF FORM FD-2892.

FOR UNCLASSIFIED COMPONENTS, PARTS, AND ACCESSORIES, NO LABELING OR OTHER INFORMATION IS REQUIRED. FOR UNCLASSIFIED SUPPORTING REAGENT SYSTEMS, ATTACH MINIMUM LABELING OR OTHER INFORMATION ADEQUATE TO DESCRIBE THE CONTENTS AND INTENDED USE OF THE REAGENT SYSTEM (SEE EXAMPLE 9A).

EXAMPLE #12



OMB No. 57-R-0128

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION
MEDICAL DEVICE LISTING

Complete and return to:
Food and Drug Administration
Bureau of Medical Devices (HFK-124)
8757 Georgia Avenue
Silver Spring, MD 20910

Note: This form is authorized by Section 510 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 360). Failure to report this information is a violation of Section 301(p) of the Act (21 U.S.C. 331(p)). Persons who violate this provision may, if convicted, be subject to a fine or imprisonment or both. The submission of any report that is false or misleading in any material respect is a violation of Section 301(q)(2), (21 U.S.C. 331(g)(2)) and may be a violation of 18 U.S.C. 1001.

1 — 7	- 14	15	16 — 21			22 — 27		
1. DOCUMENT NUMBER	2. INITIAL DOCUMENT NUMBER	3. REASON FOR SUBMISSION	4. ACTIVITY DATE			5. REPORT DATE		
			MO	DAY	YR	MO	DAY	YR
A 282512		A				09	14	77

28 L

6. OWNER/OPERATOR NAME: BEST REAGENTS INC.

29 — 35 7. OWNER/OPERATOR ID NO.: 1323456

8. CLASSIFICATION NAME: RADIOIMMUNOASSAY TOTAL THYROXINE

36 37 — 43 9. CLASSIFICATION NO.: 75 CDX

44 10. PROPRIETARY NAME: T4-RIA KIT

183

184 11. COMMON OR USUAL NAME: RIA METHOD TO DETERMINE TOTAL THYROXINE

323

12. IS THE ABOVE LISTED DEVICE THE SUBJECT OF ANY PERFORMANCE STANDARD ESTABLISHED PURSUANT TO SECTION 514 OF THE FEDERAL FOOD, DRUG, AND COSMETIC ACT OR SECTION 358 OF THE RADIATION CONTROL FOR HEALTH AND SAFETY ACT? 324 ☐ YES ☒ NO

12a. ENTER THE APPROPRIATE NAME AND SECTION NUMBER FROM CHAPTER 21 OF THIS CODE OF FEDERAL REGULATIONS. NAME: 325 — 328 SECTION 329 — 334 PARA.

13. IS THE ABOVE LISTED DEVICE THE SUBJECT OF A PREMARKET APPROVAL PURSUANT TO SECTION(S) 505, 507 OR 515 OF THE FEDERAL FOOD, DRUG AND COSMETIC ACT? 335 ☐ YES ☒ NO

13a. IDENTIFY ANY APPROVED PREMARKET APPLICATION BY ITS ASSIGNED FDA NUMBER: 336 — 345

14. IS THE DEVICE, AS LABELED, INTENDED FOR DISTRIBUTION TO AND USE BY THE GENERAL PUBLIC? 346 ☐ YES ☒ NO

28 30	31 — 37		38	39	40	41	42	43	44
SEQ	15. EST. REG. NUMBER	16. ESTABLISHMENT NAME	17. EST. TYPE						
			D	F	I	M	P	R	
501	1323456	BEST REAGENTS INC.				M			
502									
503									
504									
505									
506									

18. SIGNATURE: David C Hood

19. TYPED OR PRINTED NAME: DAVID C. HOOD

FORM FD 2892 (7/77)

LISTING AN IN VITRO DIAGNOSTIC PRODUCT FOUND ON THE CLASSIFICATION LIST. SINCE THIS REAGENT SYSTEM COULD BE USED WITH ANY GENERAL PURPOSE INSTRUMENT, RATHER THAN WITH A DEDICATED INSTRUMENT, THE REAGENT CLASSIFICATION NAME IS ENTERED IN BLOCK 8.

EXAMPLE #13

OMB No. 57-R-0128

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION
MEDICAL DEVICE LISTING

Complete and return to:
Food and Drug Administration
Bureau of Medical Devices (HFK-124)
8757 Georgia Avenue
Silver Spring, MD 20910

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1. DOCUMENT NUMBER	2. INITIAL DOCUMENT NUMBER	3. REASON FOR SUBMISSION	4. ACTIVITY DATE MO	DAY	YR	5. REPORT DATE MO	DAY	YR
A 200011		A				12	15	77

	6. OWNER/OPERATOR NAME	7. OWNER/OPERATOR ID NO.
L	KISHI OPTICAL MANUFACTURING COMPANY	FOREIGN

8. CLASSIFICATION NAME	9. CLASSIFICATION NO.
LENS, SPECTACLE, NON-CUSTOM (PRESCRIPTION)	86 HQG

10. PROPRIETARY NAME
KISHI LENS

11. COMMON OR USUAL NAME
SPECTACLE LENS BLANKS

12. IS THE ABOVE LISTED DEVICE THE SUBJECT OF ANY PERFORMANCE STANDARD ESTABLISHED PURSUANT TO SECTION 514 OF THE FEDERAL FOOD, DRUG, AND COSMETIC ACT OR SECTION 358 OF THE RADIATION CONTROL FOR HEALTH AND SAFETY ACT? ☐ YES ☒ NO

12a. ENTER THE APPROPRIATE NAME AND SECTION NUMBER FROM CHAPTER 21 OF THIS CODE OF FEDERAL REGULATIONS. NAME: SECTION PARA.

13. IS THE ABOVE LISTED DEVICE THE SUBJECT OF A PREMARKET APPROVAL PURSUANT TO SECTION(S) 505, 507 OR 515 OF THE FEDERAL FOOD, DRUG AND COSMETIC ACT? ☐ YES ☒ NO

13a. IDENTIFY ANY APPROVED PREMARKET APPLICATION BY ITS ASSIGNED FDA NUMBER:

14. IS THE DEVICE, AS LABELED, INTENDED FOR DISTRIBUTION TO AND USE BY THE GENERAL PUBLIC? ☐ YES ☒ NO

SEQ	15. EST. REG. NUMBER	16. ESTABLISHMENT NAME	17. EST. TYPE D	F	I	M	P	R
S01	NONE	KISHI OPTICAL MANUFACTURING COMPANY		F				
S02	2056789	KISHI OPTICAL, U.S.A.			I			
S03								
S04								
S05								
S06								

18. SIGNATURE	19. TYPED OR PRINTED NAME
H. Kishi	H. KISHI

FORM FD 2892 (7/77)

LISTING BY AN UNREGISTERED FOREIGN ESTABLISHMENT. ENTER "FOREIGN" IN BLOCK 7 AND "NONE" IN BLOCK 15 S 01.

SPECIAL INSTRUCTION: IF THE INITIAL DISTRIBUTOR HAS BEEN AUTHORIZED TO SUBMIT LISTING INFORMATION FOR A FOREIGN OWNER/OPERATOR, BLOCK 6, AND IF APPROPRIATE, BLOCK 7 SHALL BE THE NAME AND ID NUMBER OF THE FOREIGN OWNER/OPERATOR. DO NOT USE THE OWNER/OPERATOR NAME AND NUMBER OF THE DISTRIBUTOR IN BLOCKS 6 AND 7. INSTEAD, SHOW THIS DESIGNATION BY ENTERING THE REGISTRATION NUMBER, NAME AND THE LETTER "I" IN COLUMN I IN BLOCKS 15, 16, AND 17.

EXAMPLE #14

OMB No. 57-R-0128

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION
MEDICAL DEVICE LISTING

Complete and return to
Food and Drug Administration
Bureau of Medical Devices (HFK-124)
8757 Georgia Avenue
Silver Spring, MD 20910

Note: This form is authorized by Section 510 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 360). Failure to report this information is a violation of Section 301(p) of the Act (21 U.S.C. 331(p)). Persons who violate this provision may, if convicted, be subject to a fine or imprisonment or both. The submission of any report that is false or misleading in any material respect is a violation of Section 301(q)(2), (21 U.S.C. 331(g)(2))and may be a violation of 18 U.S.C. 1001.

1. DOCUMENT NUMBER	2. INITIAL DOCUMENT NUMBER	3. REASON FOR SUBMISSION	4. ACTIVITY DATE MO	DAY	YR	5. REPORT DATE MO	DAY	YR
A 282514	A 200031	C	08	15	78	09	15	78

L

6. OWNER/OPERATOR NAME: HEMATOLOGY RESEARCH LAB

7. OWNER OPERATOR ID NO.: 1112345

8. CLASSIFICATION NAME: FIBRIN, FITC, ANTIGEN, ANTISERUM, CONTROL

9. CLASSIFICATION NO.: 82 DBB

10. PROPRIETARY NAME: FIBRIN ANALYSIS KIT

11. COMMON OR USUAL NAME:

12. IS THE ABOVE LISTED DEVICE THE SUBJECT OF ANY PERFORMANCE STANDARD ESTABLISHED PURSUANT TO SECTION 514 OF THE FEDERAL FOOD, DRUG, AND COSMETIC ACT OR SECTION 358 OF THE RADIATION CONTROL FOR HEALTH AND SAFETY ACT? ☐ YES ☒ NO

12a. ENTER THE APPROPRIATE NAME AND SECTION NUMBER FROM CHAPTER 21 OF THIS CODE OF FEDERAL REGULATIONS. **NAME:** SECTION PARA.

13. IS THE ABOVE LISTED DEVICE THE SUBJECT OF A PREMARKET APPROVAL PURSUANT TO SECTION(S) 505, 507 OR 515 OF THE FEDERAL FOOD, DRUG AND COSMETIC ACT? ☐ YES ☒ NO

13a. IDENTIFY ANY APPROVED PREMARKET APPLICATION BY ITS ASSIGNED FDA NUMBER:

14. IS THE DEVICE, AS LABELED, INTENDED FOR DISTRIBUTION TO AND USE BY THE GENERAL PUBLIC? ☐ YES ☒ NO

SEQ	15. EST. REG. NUMBER	16. ESTABLISHMENT NAME	17. EST. TYPE D	F	I	M	P	R
S01	1112345	HEMATOLOGY RESEARCH LAB	D			M		
S02	1012345	HEMATOLOGY RESEARCH LAB					P	
S03								
S04								
S05								
S06								

18. SIGNATURE: Frank Smith

19. TYPED OR PRINTED NAME: FRANK SMITH

FORM FD 2892 (7/77)

TO UPDATE A DEVICE PREVIOUSLY LISTED (SEE EXAMPLE 1 FOR INITIAL LISTING), ALL INFORMATION ON THE FORM FD-2892 MUST BE COMPLETED. ENTER THE INITIAL DOCUMENT NUMBER IN BLOCK 2, ENTER "C" IN BLOCK 3 TO INDICATE A CHANGE WHICH IS TO ADD AN ADDITIONAL ESTABLISHMENT SITE IN LINE S 02.

EXAMPLE #15

OMB No. 57-R-0128

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION
MEDICAL DEVICE LISTING

Complete and return to:
Food and Drug Administration
Bureau of Medical Devices (HFK-124)
8757 Georgia Avenue
Silver Spring, MD 20910

Note: This form is authorized by Section 510 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 360). Failure to report this information is a violation of Section 301(p) of the Act (21 U.S.C. 331(p)). Persons who violate this provision may, if convicted, be subject to a fine or imprisonment or both. The submission of any report that is false or misleading in any material respect is a violation of Section 301(q)(2), (21 U.S.C. 331(g)(2))and may be a violation of 18 U.S.C. 1001.

1. DOCUMENT NUMBER	2. INITIAL DOCUMENT NUMBER	3. REASON FOR SUBMISSION	4. ACTIVITY DATE MO	DAY	YR	5. REPORT DATE MO	DAY	YR.
A 200027	A 200014	D	03	31	78	04	01	78

	6. OWNER/OPERATOR NAME	7. OWNER/OPERATOR ID NO.
L	DOCTOR'S BEST DEVICES	9831001

8. CLASSIFICATION NAME: RONGEUR, ORTHOPEDIC

9. CLASSIFICATION NO.: 87 HTX

10. PROPRIETARY NAME:

11. COMMON OR USUAL NAME:

12. IS THE ABOVE LISTED DEVICE THE SUBJECT OF ANY PERFORMANCE STANDARD ESTABLISHED PURSUANT TO SECTION 514 OF THE FEDERAL FOOD, DRUG, AND COSMETIC ACT OR SECTION 358 OF THE RADIATION CONTROL FOR HEALTH AND SAFETY ACT? ☐ YES ☐ NO

12a. ENTER THE APPROPRIATE NAME AND SECTION NUMBER FROM CHAPTER 21 OF THIS CODE OF FEDERAL REGULATIONS. NAME: SECTION PARA.

13. IS THE ABOVE LISTED DEVICE THE SUBJECT OF A PREMARKET APPROVAL PURSUANT TO SECTION(S) 505, 507 OR 515 OF THE FEDERAL FOOD, DRUG AND COSMETIC ACT? ☐ YES ☐ NO

13a. IDENTIFY ANY APPROVED PREMARKET APPLICATION BY ITS ASSIGNED FDA NUMBER:

14. IS THE DEVICE, AS LABELED, INTENDED FOR DISTRIBUTION TO AND USE BY THE GENERAL PUBLIC? ☐ YES ☐ NO

SEQ	15. EST. REG. NUMBER	16. ESTABLISHMENT NAME	17. EST. TYPE D	F	I	M	P	R
S01								
S02								
S03								
S04								
S05								
S06								

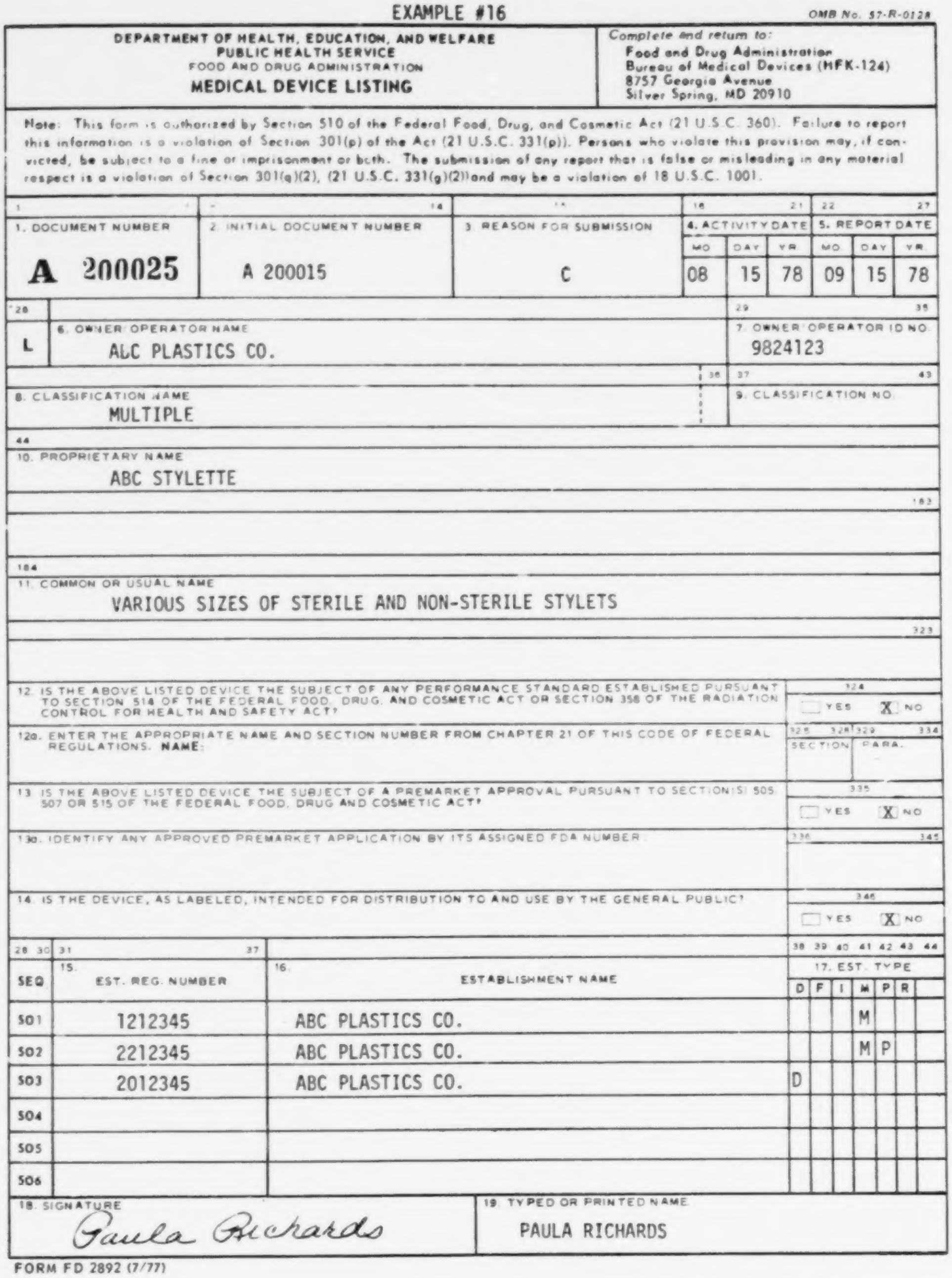
18. SIGNATURE: Mary Jones

19. TYPED OR PRINTED NAME: MARY JONES

FORM FD 2892 (7/77)

TO DISCONTINUE ALL THE DEVICES LISTED UNDER ONE CLASSIFICATION NAME (SEE EXAMPLE 3 FOR INITIAL LISTING), ENTER THE INITIAL DOCUMENT NUMBER IN BLOCK 2, ENTER "D" IN BLOCK 3, AND DISCONTINUANCE DATE IN BLOCK 4. IN ADDITION, COMPLETE BLOCKS 5 THROUGH 9 AND 18 AND 19.

EXAMPLE #16



OMB No. 57-R-0128

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION
MEDICAL DEVICE LISTING

Complete and return to:
Food and Drug Administration
Bureau of Medical Devices (HFK-124)
8757 Georgia Avenue
Silver Spring, MD 20910

Note: This form is authorized by Section 510 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 360). Failure to report this information is a violation of Section 301(p) of the Act (21 U.S.C. 331(p)). Persons who violate this provision may, if convicted, be subject to a fine or imprisonment or both. The submission of any report that is false or misleading in any material respect is a violation of Section 301(q)(2), (21 U.S.C. 331(g)(2)) and may be a violation of 18 U.S.C. 1001.

1. DOCUMENT NUMBER	2. INITIAL DOCUMENT NUMBER	3. REASON FOR SUBMISSION	4. ACTIVITY DATE MO	DAY	YR	5. REPORT DATE MO	DAY	YR
A 200025	A 200015	C	08	15	78	09	15	78

28	6. OWNER/OPERATOR NAME	7. OWNER/OPERATOR ID NO.
L	ALC PLASTICS CO.	9824123

8. CLASSIFICATION NAME: MULTIPLE

9. CLASSIFICATION NO.:

10. PROPRIETARY NAME: ABC STYLETTE

11. COMMON OR USUAL NAME: VARIOUS SIZES OF STERILE AND NON-STERILE STYLETS

12. IS THE ABOVE LISTED DEVICE THE SUBJECT OF ANY PERFORMANCE STANDARD ESTABLISHED PURSUANT TO SECTION 514 OF THE FEDERAL FOOD, DRUG, AND COSMETIC ACT OR SECTION 358 OF THE RADIATION CONTROL FOR HEALTH AND SAFETY ACT? ☐ YES ☒ NO

12a. ENTER THE APPROPRIATE NAME AND SECTION NUMBER FROM CHAPTER 21 OF THIS CODE OF FEDERAL REGULATIONS. **NAME:** SECTION PARA.

13. IS THE ABOVE LISTED DEVICE THE SUBJECT OF A PREMARKET APPROVAL PURSUANT TO SECTION(S) 505, 507 OR 515 OF THE FEDERAL FOOD, DRUG AND COSMETIC ACT? ☐ YES ☒ NO

13a. IDENTIFY ANY APPROVED PREMARKET APPLICATION BY ITS ASSIGNED FDA NUMBER:

14. IS THE DEVICE, AS LABELED, INTENDED FOR DISTRIBUTION TO AND USE BY THE GENERAL PUBLIC? ☐ YES ☒ NO

SEQ	15. EST. REG. NUMBER	16. ESTABLISHMENT NAME	17. EST. TYPE D	F	I	M	P	R	
501	1212345	ABC PLASTICS CO.				M			
502	2212345	ABC PLASTICS CO.				M	P		
503	2012345	ABC PLASTICS CO.	D						
504									
505									
506									

18. SIGNATURE: Paula Richards

19. TYPED OR PRINTED NAME: PAULA RICHARDS

FORM FD 2892 (7/77)

UPDATING A DEVICE WITH MULTIPLE CLASSIFICATION NAMES (SEE EXAMPLE 6 FOR INITIAL LISTING). ENTER THE INITIAL DOCUMENT NUMBER IN BLOCK 2, ENTER "C" IN BLOCK 3 TO INDICATE A CHANGE WHICH IN THIS CASE IS ADDING A CLASSIFICATION NAME AND DELETING A PREVIOUSLY LISTED CLASSIFICATION NAME. ENTER THE DATE OF THE CHANGE IN BLOCK 4.

SHOW THE CHANGES ON THE SUPPLEMENTAL SHEET (SEE EXAMPLE 16A).

EXAMPLE #16A

DOC. NO. A 200025

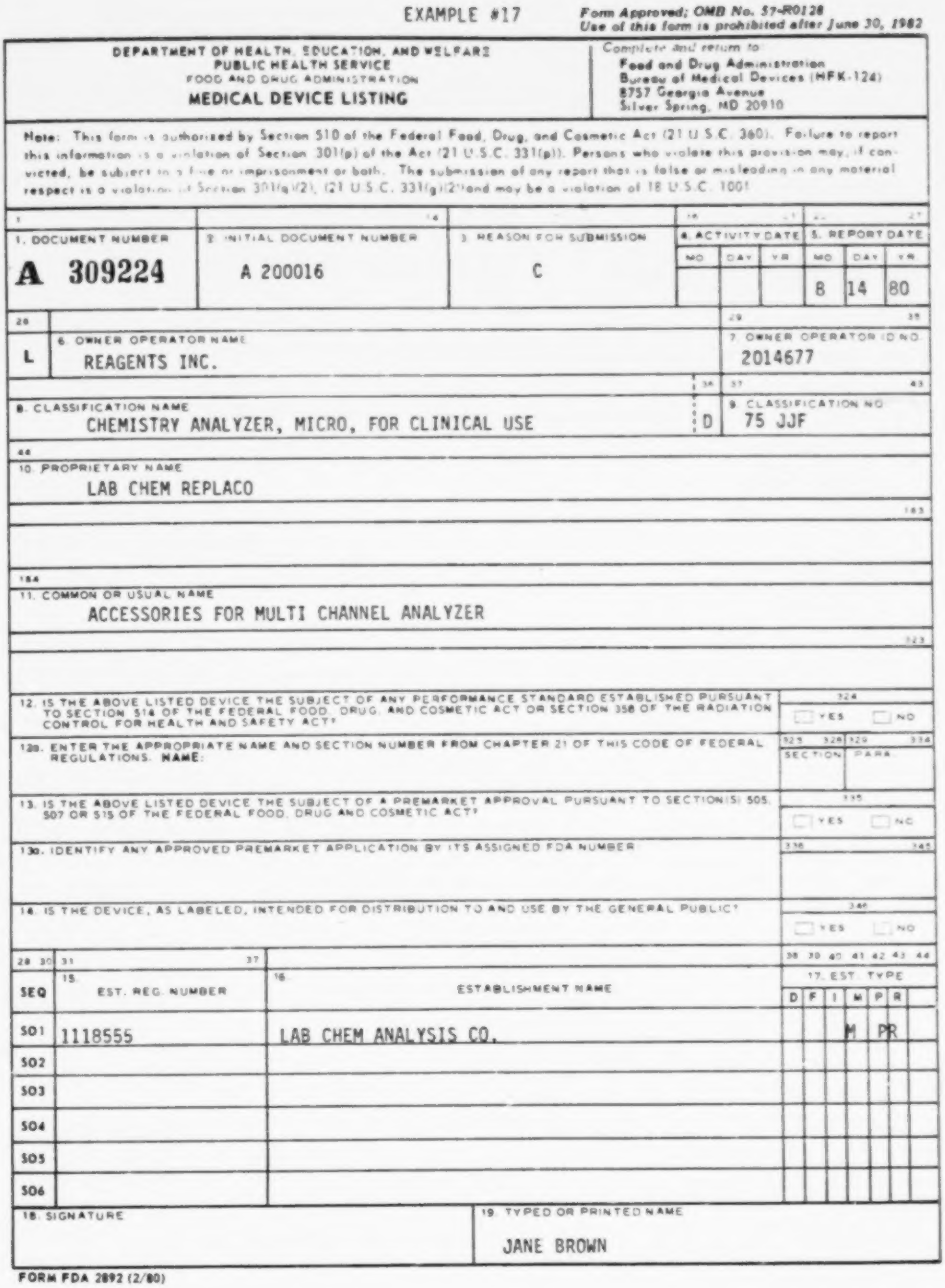
ABC PLASTICS COMPANY
12 KING STREET
BOSTON, MA 02115

DEVICE NAMES

1.	STYLET, SURGICAL, GENERAL AND PLASTIC SURGERY	79 GAH	
2.	STYLET, TRACHEAL TUBE	73 BSR	
3.	STYLET, URETERAL	78 EYA	ADDED
~~4.~~	~~STYLET, FOR CATHETER, GASTRO UROLOGY~~	~~78 DZB~~	DELETED

NOTE: DOCUMENT NUMBER ON THE UPPER RIGHT HAND CORNER SHOULD BE THE NUMBER IN BLOCK 1 NOT THE NUMBER IN BLOCK 2.

THIS SUPPLEMENTAL SHEET IS TO UPDATE EXAMPLE 6A BY DELETING ONE OF THE CLASSIFICATION NAMES AND ADDING ANOTHER TO A PREVIOUSLY LISTED DEVICE.



EXAMPLE #17

Form Approved; OMB No. 57-R0128
Use of this form is prohibited after June 30, 1982

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION
MEDICAL DEVICE LISTING

Complete and return to:
Food and Drug Administration
Bureau of Medical Devices (HFK-124)
8757 Georgia Avenue
Silver Spring, MD 20910

Note: This form is authorized by Section 510 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 360). Failure to report this information is a violation of Section 301(p) of the Act (21 U.S.C. 331(p)). Persons who violate this provision may, if convicted, be subject to a fine or imprisonment or both. The submission of any report that is false or misleading in any material respect is a violation of Section 301(q)(2), (21 U.S.C. 331(q)(2)) and may be a violation of 18 U.S.C. 1001

1. DOCUMENT NUMBER	2. INITIAL DOCUMENT NUMBER	3. REASON FOR SUBMISSION	4. ACTIVITY DATE			5. REPORT DATE		
			MO	DAY	YR	MO	DAY	YR
A 309224	A 200016	C				8	14	80

L	6. OWNER OPERATOR NAME REAGENTS INC.	7. OWNER OPERATOR ID NO. 2014677
8. CLASSIFICATION NAME CHEMISTRY ANALYZER, MICRO, FOR CLINICAL USE	D	9. CLASSIFICATION NO. 75 JJF

10. PROPRIETARY NAME
LAB CHEM REPLACO

11. COMMON OR USUAL NAME
ACCESSORIES FOR MULTI CHANNEL ANALYZER

12. IS THE ABOVE LISTED DEVICE THE SUBJECT OF ANY PERFORMANCE STANDARD ESTABLISHED PURSUANT TO SECTION 514 OF THE FEDERAL FOOD, DRUG, AND COSMETIC ACT OR SECTION 358 OF THE RADIATION CONTROL FOR HEALTH AND SAFETY ACT? ☐ YES ☐ NO

12a. ENTER THE APPROPRIATE NAME AND SECTION NUMBER FROM CHAPTER 21 OF THIS CODE OF FEDERAL REGULATIONS. **NAME:** SECTION PARA.

13. IS THE ABOVE LISTED DEVICE THE SUBJECT OF A PREMARKET APPROVAL PURSUANT TO SECTION(S) 505, 507 OR 515 OF THE FEDERAL FOOD, DRUG AND COSMETIC ACT? ☐ YES ☐ NO

13a. IDENTIFY ANY APPROVED PREMARKET APPLICATION BY ITS ASSIGNED FDA NUMBER

14. IS THE DEVICE, AS LABELED, INTENDED FOR DISTRIBUTION TO AND USE BY THE GENERAL PUBLIC? ☐ YES ☐ NO

SEQ	15. EST. REG. NUMBER	16. ESTABLISHMENT NAME	17. EST. TYPE D	F	I	M	P	R
501	1118555	LAB CHEM ANALYSIS CO.				M	P	R
502								
503								
504								
505								
506								

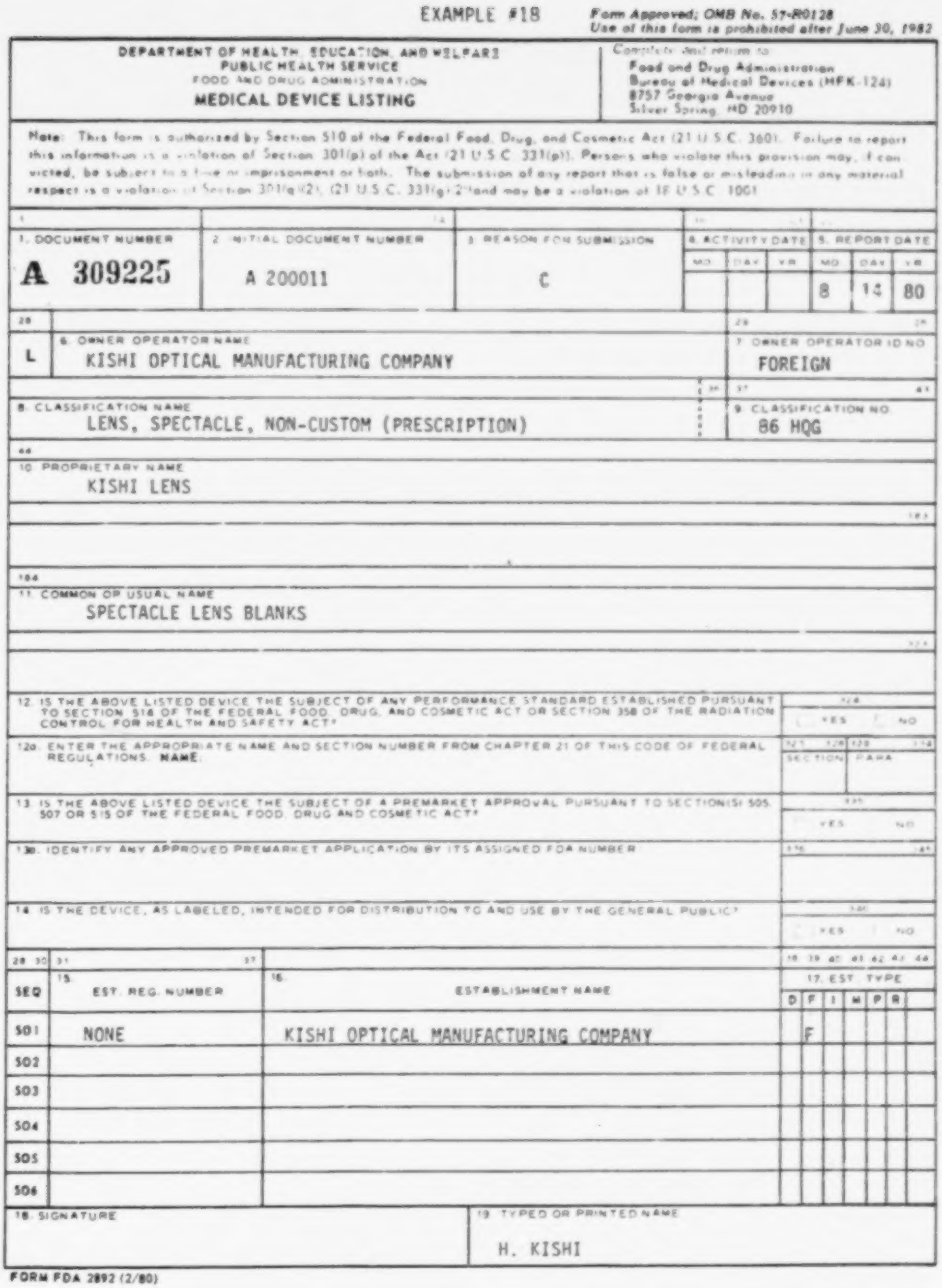
18. SIGNATURE

19. TYPED OR PRINTED NAME
JANE BROWN

FORM FDA 2892 (2/80)

EXAMPLE #17

TO UPDATE A DEVICE PREVIOUSLY LISTED (EXAMPLE #11) WHERE A CHANGE HAS OCCURRED IN OWNERSHIP. ENTER THE INITIAL DOCUMENT NUMBER IN BLOCK 2, ENTER "C" IN BLOCK 3 TO INDICATE A CHANGE. ALL INFORMATION ON FORM FD-2892 MUST BE COMPLETED.



EXAMPLE #18

Form Approved; OMB No. 57-R0128
Use of this form is prohibited after June 30, 1982

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION
MEDICAL DEVICE LISTING

Complete and return to:
Food and Drug Administration
Bureau of Medical Devices (HFK-124)
8757 Georgia Avenue
Silver Spring, MD 20910

Note: This form is authorized by Section 510 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 360). Failure to report this information is a violation of Section 301(p) of the Act (21 U.S.C. 331(p)). Persons who violate this provision may, if convicted, be subject to a fine or imprisonment or both. The submission of any report that is false or misleading in any material respect is a violation of Section 301(q)(2), (21 U.S.C. 331(q)(2)) and may be a violation of 18 U.S.C. 1001

1. DOCUMENT NUMBER	2. INITIAL DOCUMENT NUMBER	3. REASON FOR SUBMISSION	4. ACTIVITY DATE MO	DAY	YR	5. REPORT DATE MO	DAY	YR
A 309225	A 200011	C				8	14	80

L

6. OWNER OPERATOR NAME: KISHI OPTICAL MANUFACTURING COMPANY

7. OWNER OPERATOR ID NO: FOREIGN

8. CLASSIFICATION NAME: LENS, SPECTACLE, NON-CUSTOM (PRESCRIPTION)

9. CLASSIFICATION NO: 86 HQG

10. PROPRIETARY NAME: KISHI LENS

11. COMMON OR USUAL NAME: SPECTACLE LENS BLANKS

12. IS THE ABOVE LISTED DEVICE THE SUBJECT OF ANY PERFORMANCE STANDARD ESTABLISHED PURSUANT TO SECTION 514 OF THE FEDERAL FOOD, DRUG, AND COSMETIC ACT OR SECTION 358 OF THE RADIATION CONTROL FOR HEALTH AND SAFETY ACT? ☐ YES ☐ NO

12a. ENTER THE APPROPRIATE NAME AND SECTION NUMBER FROM CHAPTER 21 OF THIS CODE OF FEDERAL REGULATIONS. **NAME**: SECTION PARA

13. IS THE ABOVE LISTED DEVICE THE SUBJECT OF A PREMARKET APPROVAL PURSUANT TO SECTION(S) 505, 507 OR 515 OF THE FEDERAL FOOD, DRUG AND COSMETIC ACT? ☐ YES ☐ NO

13a. IDENTIFY ANY APPROVED PREMARKET APPLICATION BY ITS ASSIGNED FDA NUMBER

14. IS THE DEVICE, AS LABELED, INTENDED FOR DISTRIBUTION TO AND USE BY THE GENERAL PUBLIC? ☐ YES ☐ NO

SEQ	15. EST. REG. NUMBER	16. ESTABLISHMENT NAME	17. EST. TYPE D	F	I	M	P	R
501	NONE	KISHI OPTICAL MANUFACTURING COMPANY		F				
502								
503								
504								
505								
506								

18. SIGNATURE

19. TYPED OR PRINTED NAME: H. KISHI

FORM FDA 2892 (2/80)

EXAMPLE #18

TO UPDATE A DEVICE PREVIOUSLY LISTED (SEE EXAMPLE #13) TO DELETE AN ESTABLISHMENT SITE. ENTER THE INITIAL DOCUMENT NUMBER IN BLOCK 2, ENTER "C" IN BLOCK 3 TO INDICATE A CHANGE. ALL INFORMATION ON FORM FD-2892 MUST BE COMPLETED.

5 PREMARKET NOTIFICATION: 510(k)

INTRODUCTION 5- 1
FINAL RULE: PREMARKET NOTIFICATION (21 CFR 807) 5- 5
510(k) PREAMBLE (42 FR 42520) 5- 9
PREMARKET NOTIFICATION REVIEW PROGRAM 5-18
MEDICAL DEVICE EXEMPTIONS 5-33
APPENDIXES 5-45
  A. Sample Premarket Notification Letters 5-46
  B. 510(k) Response Letters 5-55
  C. Premarket Notifications: The First 24,000 5-58

INTRODUCTION

The Medical Device Amendments to the Food. Drug. and Cosmetic (FD&C) Act were enacted on May 28. 1976. They direct FDA to issue regulations that classify all devices that were in commercial distribution at that time into one of three regulatory control categories. Class I. II. or III. depending upon the degree of regulation necessary to provide reasonable assurance of their safety and effectiveness. The class into which a device is placed determines the requirements that must be met before a manufacturer may distribute the device in interstate commerce. Section 510(k) of the Medical Device Amendments to the FD&C Act contain a premarket notification [510(k)] requirement. Manufacturers intending to market a new or significantly modified device are required to submit a premarket notification to the Food and Drug Administration (FDA) in order to establish substantial equivalence (SE) in terms of safety and effectiveness to a device already on the market in the United States prior to the May 28. 1976 enactment date of these Amendments or to a device marketed after that date that has been determined substantially equivalent. The 510(k) applies to postenactment devices. i.e.. devices introduced into commercial distribution after May 28. 1976. (This requirement is not applicable to transitional devices or some Class I devices exempt by regulation.)

In brief. the premarket notification program is meant to:

- identify new devices that must be placed automatically into Class III and undergo premarket approval (PMA) or reclassification before they are marketed;
- classify new devices; a not substantially equivalent (NSE) new device is in Class III. and a substantially equivalent (SE) new device is in the same regulatory class as the device to which it is found equivalent: and
- achieve marketing equity by allowing manufacturers of new devices that are SE to preamendments devices to market their devices without facing any greater regulatory burdens than faced by manufacturers of the preamendments devices.

Premarket notification is required whenever:

- a device is being introduced into the market for the first time.
- a new device or product line is being introduced that may already be marketed by another manufacturer.
- a device currently in (or being reintroduced into) commercial distribution is about to be significantly changed or modified. or

- there is a change in the intended use of a device.

Regardless of the type of device, its manufacturer is required to submit a premarket notification to the Center for Devices and Radiological Health (CDRH) at least 90 days before introducing the device into interstate commerce or otherwise holding or offering the device for commercial distribution.

CDRH will determine whether the device is substantially equivalent to a device that was or is being marketed. If the device is determined to be equivalent, then it can be marketed. If CDRH determines that a device is nonequivalent, the manufacturer may resubmit another 510(k) with new data, file a reclassification petition, or submit a premarket approval (PMA) application.

The determination of substantial equivalence is made within 90 days of receipt of a premarket notification. The decision is made by scientific staff of the CDRH, based upon information submitted by the manufacturer in the premarket notification and other information available to the Food and Drug Administration (FDA). A premarket notification must include, among other items [as specified in 21 Code of Federal Regulations (CFR) Part 807, Subpart E], the proposed labeling for the device which must be in sufficient detail to describe the device (including technical specifications), its intended use, and directions for use.

Typically, a reviewer initially determines whether the device performs the same function and falls within an established type of device which was introduced to interstate commerce for commercial distribution before May 28, 1976 (preamendment). The review of the premarket notification then compares the characteristics of the "new" device (designs, material, energy source, etc.) to the characteristics of the preamendments device. If the differences do not raise new types of safety and effectiveness questions for the same intended use, the new device is found equivalent.

There is no requirement that an actual prototype of a device must be manufactured. In some cases, however, data from actual device testing are necessary to demonstrate substantial equivalence; thus, working models are needed to obtain these data. The need for detailed functional data depends on what is further needed to demonstrate equivalence and on the complexity of the device. For example, it is likely that little or no functional data would be needed to determine equivalence of a simple, hand-held manual instrument that has minor differences in configuration. In contrast, considerable data may be necessary to judge the equivalence of different manufacturers' implantable cardiac pacemakers.

The purpose of data, such as clinical data, for a premarket notification submission is to demonstrate that the device is equivalent in performance to the preamendments device. FDA does not intend that the data determine the device's safety and effectiveness. Premarket notification does, nonetheless, provide some degree of public protection by allowing FDA to "screen out" devices that:

- present significant **unanswered** questions of safety and effectiveness relative to their preamendment predecessors;
- appear to be less safe or effective than their preamendments predecessors; or
- have indications for use or technology sufficiently different from preamendment devices so that adequate comparisons are impossible.

The collection of clinical data involving human subjects in support of premarket notification must comply with the requirements of the Investigational Device Exemption (IDE) regulations found in 21 CFR Part 812.

A premarket notification must be submitted in duplicate on standard size paper securely bound. if necessary. There is no prescribed form for a premarket notification submission. but it should be designated in the cover letter as "510(k) notification."

> [For the kinds of information usually required. see the five sample 510(k) premarket notification cover letters contained in this booklet.]

CDRH has 90 days to determine substantial equivalence. This period begins when CDRH logs in the 510(k) submission and can only be altered:

- o by a request for additional information from FDA. or
- o at the request of the submitter who may for varying reasons wish to withdraw the submission.

When additional information is requested by a CDRH scientific reviewer. the 510(k) file is put on hold and a letter is issued from the Premarket Notification Coordinator stating that the file will be retained for 30 days. while awaiting the submitter's response. If a response is not received within 30 days. the 510(k) will be considered withdrawn. The submitter has the option of submitting the requested information within 30 days. requesting an extension of the 30-day period. requesting that the 510(k) be withdrawn, or doing nothing. When CDRH receives the additional information. the 90-day review period begins again. This happens each time additional information is requested.

If a manufacturer has submitted a 510(k) but they have not heard from CDRH for 90 days. technically. the manufacturer has met the requirements of Section 510(k) of the FD&C Act. 21 CFR Part 807.81. and may market the device covered by the 510(k) submission subject to other provisions of the Act and other Federal regulations. (See the accompanying 510(k) Regulation and Preamble.) This is not. however. an admission by FDA that the product is substantially equivalent.

FDA may continue the review of the submission beyond the 90-day period and conclude that the device is not substantially equivalent to a device that was marketed in interstate commerce before May 28. 1976. or to a device that has been reclassified into Class I or II. In this situation it would be necessary to remove the device from the market. We. therefore. recommend that manufacturers **do not market** a device before FDA has made a final decision. Most reviews are completed within the 90-day period.

If you do not receive a decision within 90 days. it would be prudent to check with FDA to make certain that the submission was received and acted upon. DSMA's services include checking up on such problems. Call 800-638-2041 or (301) 443-6597.

When a manufacturer and CDRH disagree about substantial equivalence of a device. the following applies:

- o Final determination of this issue remains with FDA. A device that FDA finds to be not substantially equivalent is automatically classified into Class III. and unless reclassified. is subject to premarket approval.

- Under Section 513(f) of the Act, a manufacturer may petition FDA for reclassification of this device into Class I or Class II. FDA will find such a petition to be acceptable for filing only if it contains sufficient data to justify the request for reclassification.

Manufacturers of preamendment Class III devices and of substantially equivalent postamendment Class III devices may continue to market them until a PMA is required. A PMA cannot be required earlier than 30 months after the effective date of final classification of a device into Class III.

There are no substitute procedures for meeting premarket notification requirements. Submission of a device registration form FDA-2891 or device listing form FDA-2892 does not fulfill the requirements for premarket notification.

The manufacturer is responsible for determining if a proposed device change or modification warrants submission of a 510(k). It is not FDA's intent that a 510(k) must be submitted for every change in design, material, chemical composition, energy source, or manufacturing process, but only where such changes could significantly affect safety or effectiveness of the device. FDA believes that the manufacturer is best qualified to make this determination, which should be based on the exercise of good judgment, adequate supporting data, and sufficient documentation.

If, after attempting to evaluate the change, manufacturers are still uncertain about the need for a 510(k), they may contact the appropriate device evaluation group at CDRH and speak to a reviewer, or consult DSMA at 800-638-2041 or (301) 443-6597.

FDA will observe confidentiality of the existence of a 510(k) for a period of 90 days from receipt of the submission in those cases where:

- the device is not on the market,
- the intent to market the device has not been previously disclosed, and
- the firm requests in its 510(k) that FDA treat the submission of the firm's intent to market as confidential information.

Requests for confidentiality must state that:

- the intent to market the device is confidential,
- the intent to market has not been revealed,
- the confidentiality of the firm's intent to market has been protected by the firm,
- the firm will notify FDA when the intent to market the device is disclosed or the device is put on the market, and
- the firm understands the prohibition against submitting false information to the Government.

[For an example of an adequate request for confidentiality and the accompanying statement, see sample 510(k) letters #2 and #5 in the appendix of this chapter.]

21 CFR 807
PREMARKET NOTIFICATION: 510(k)
(FR 8/23/77)

Final Rule

PART 807—ESTABLISHMENT REGISTRATION AND DEVICE LISTING FOR MANUFACTURERS OF DEVICES

Subpart A—General Provisions

Sec.
807.3 Definitions.

Subpart B—Procedures for Domestic Device Establishments

807.20 Who must register and submit a device list.
807.21 Times for establishment registration and device listing.
807.22 How and where to register establishments and list devices.
807.25 Information required or requested for establishment registration and device listing.
807.26 Amendments to establishment registration.
807.30 Updating device listing information.
807.31 Additional listing information.
807.35 Notification of registrant.
807.37 Inspection of establishment registration and device listings.
807.39 Misbranding by reference to establishment registration or to registration number.

Subpart C—Registration Procedures for Foreign Device Establishments

807.40 Establishment registration and device listing for foreign manufacturers of devices.

Subpart D—Exemptions

807.65 Exemptions for device establishments.

Subpart E—Premarket Notification Procedures

807.81 When a premarket notification submission is required.
807.85 Exemption from premarket notification.
807.87 Information required in a premarket notification submission.
807.90 Format of a premarket notification submission.
807.95 Confidentiality of information.
807.97 Misbranding by reference to premarket notification.

AUTHORITY: Secs. 301(p), 501, 502, 510, 513, 701(a), 52 Stat. 1049-1051 as amended, 1055, 76 Stat. 794-795 as amended, 86 Stat. 462 as amended, 90 Stat. 540-546 (21 U.S.C. 331(p), 351, 352, 360, 360c, 371(a)); 21 CFR 5.10.

SOURCE: 42 FR 42526, Aug. 23, 1977, unless otherwise noted.

Subpart E—Premarket Notification Procedures

§ 807.81 When a premarket notification submission is required.

(a) Except as provided in paragraph (b) of this section, each person who is required to register his establishment pursuant to § 807.20 must submit a premarket notification submission to the Food and Drug Administration at least 90 days before he proposes to begin the introduction or delivery for introduction into interstate commerce for commercial distribution of a device intended for human use which meets any of the following criteria:

(1) The device is being introduced into commercial distribution for the first time; that is, the device is not of the same type as, or is not substantially equivalent to, (i) a device in commercial distribution before May 28, 1976, or (ii) a device introduced for commercial distribution after May 28, 1976, that has subsequently been reclassified into class I or II.

(2) The device is being introduced into commercial distribution for the first time by a person required to register, whether or not the device meets the criteria in paragraph (a)(1) of this section.

(3) The device is one that the person currently has in commercial distribution or is reintroducing into commercial distribution, but that is about to be significantly changed or modified in design, components, method of manufacture, or intended use. The following constitute significant changes or modifications that require a premarket notification:

(i) A change or modification in the device that could significantly affect the safety or effectiveness of the device, e.g., a significant change or modification in design, material, chemical composition, energy source, or manufacturing process.

(ii) A major change or modification in the intended use of the device.

(b) A premarket notification under this subpart is not required for a device for which a premarket approval application under section 515 of the act, or for which a petition to reclassify under section 513(f)(2) of the act, is pending before the Food and Drug Administration.

(c) In addition to complying with the requirements of this part, owners or operators of device establishments that manufacture radiation-emitting electronic products, as defined in § 1000.3 of this chapter, shall comply with the reporting requirements of Part 1002 of this chapter.

§ 807.85 Exemption from premarket notification.

(a) A device is exempt from the premarket notification requirements of this subpart if the device intended for introduction into commercial distribution is not generally available in finished form for purchase and is not offered through labeling or advertising by the manufacturer, importer, or distributor thereof for commercial distribution, and the device meets one of the following conditions:

(1) It is intended for use by a patient named in the order of the physician or dentist (or other specially qualified person); or

(2) It is intended solely for use by a physician or dentist (or other specially qualified person) and is not generally available to, or generally used by, other physicians or dentists (or other specially qualified persons).

(b) A distributor who places a device into commercial distribution for the first time under his own name and a repackager who places his own name on a device and does not change any other labeling or otherwise affect the device shall be exempted from the premarket notification requirements of this subpart if:

(1) The device was in commercial distribution before May 28, 1976; or

(2) A premarket notification submission was filed by another person.

§ 807.87 Information required in a premarket notification submission.

Each premarket notification submission shall contain the following information:

(a) The device name, including both the trade or proprietary name and the common or usual name or classification name of the device.

(b) The establishment registration number, if applicable, of the owner or operator submitting the premarket notification submission.

(c) The class in which the device has been put under section 513 of the act and, if known, its appropriate panel; or, if the owner or operator determines that the device has not been classified under such section, a statement of that determination and the basis for the person's determination that the device is not so classified.

(d) Action taken by the person required to register to comply with the requirements of the act under section 514 for performance standards.

(e) Proposed labels, labeling, and advertisements sufficient to describe the device, its intended use, and the directions for its use. Where applicable, photographs or engineering drawings should be supplied.

(f) A statement indicating the device is similar to and/or different from other products of comparable type in commercial distribution, accompanied by data to support the statement. This information may include an identification of similar products, materials, design considerations, energy expected to be used or delivered by the device, and a description of the operational principles of the device.

(g) Where a person required to register intends to introduce into commercial distribution a device that has undergone a significant change or modification that could significantly affect the safety or effectiveness of the device, or the device is to be marketed for a new or different indication for use, the premarket notification submission must include appropriate supporting data to show that the manufacturer has considered what consequences and effects the change or modification or new use might have on the safety and effectiveness of the device.

(h) Any additional information regarding the device requested by the Commissioner that is necessary for the Commissioner to make a finding as to whether or not the device is substantially equivalent to a device in commercial distribution. A request for additional information will advise the owner or operator that there is insufficient information contained in the original premarket notification submission for the Commissioner to make this determination and that the owner or operator may either submit the requested data or a new premarket notification containing the requested information at least 90 days before the owner or operator intends to market the device, or submit a premarket approval application in accordance with section 515 of the act. If the additional information is not submitted within 30 days following the date of the request, the Commissioner will consider the premarket notification to be withdrawn.

§ 807.90 Format of a premarket notification submission.

Each premarket notification submission pursuant to this part shall be submitted in accordance with this section. Each submission shall:

(a) Be addressed to the Food and Drug Administration, Bureau of Medical Devices (HFK-20), 8757 Georgia Ave., Silver Spring, Md. 20910. All inquiries regarding a premarket notification submission should be in writing and sent to the above address.

(b) Be bound into a volume or volumes, where necessary.

(c) Be submitted in duplicate on standard size paper, including the original and two copies of the cover letter.

(d) Be submitted separately for each product the manufacturer intends to market.

(e) Designated "510(k) Notification" in the cover letter.

§ 807.95 Confidentiality of information.

(a) The Food and Drug Administration will disclose publicly whether there exists a premarket notification submission under this part:

(1) Where the device is on the market, i.e., introduced or delivered for introduction into interstate commerce for commercial distribution;

(2) Where the person submitting the premarket notification submission has disclosed, through advertising or any other manner, his intent to market the device to scientists, market analysts, exporters, or other individuals who are not employees of, or paid consultants to, the establishment and who are not in an advertising or law firm pursuant to commercial arrangements with appropriate safeguards for secrecy; or

(3) Where the device is not on the market and the intent to market the device has not been so disclosed, except where the submission is subject to an exception under paragraph (b) or (c) of this section.

(b) The Food and Drug Administration will not disclose publicly the existence of a premarket notification submission for a device that is not on the market and where the intent to market the device has not been disclosed for 90 days from the date of receipt of the submission, if:

(1) The person submitting the premarket notification submission requests in the submission that the Food and Drug Administration hold as confidential commercial information the intent to market the device and submits a written certification to the Commissioner:

(i) That the person considers his intent to market the device to be confidential commercial information;

(ii) That neither the person nor, to the best of his knowledge, anyone else, has disclosed through advertising or any other manner, his intent to market the device to scientists, market analysts, exporters, or other individuals, except employees of, or paid consultants to, the establishment or individuals in an advertising or law firm pursuant to commercial arrangements with appropriate safeguards for secrecy;

(iii) That the person will immediately notify the Food and Drug Administration if he discloses the intent to market the device to anyone, except employees of, or paid consultants to, the establishment or individuals in an advertising or law firm pursuant to commercial arrangements with appropriate safeguards for secrecy;

(iv) That the person has taken precautions to protect the confidentiality of the intent to market the device; and

(v) That the person understands that the submission to the government of false information is prohibited by 18 U.S.C. 1001 and 21 U.S.C. 331(q); and

(2) The Commissioner agrees that the intent to market the device is confidential commercial information.

(c) Where the Commissioner determines that the person has complied with the procedures described in paragraph (b) of this section with respect to a device that is not on the market and where the intent to market the device has not been disclosed, and the Commissioner agrees that the intent to market the device is confidential commercial information, the Commissioner will not disclose the existence of the submission for 90 days from the date of its receipt by the agency. In addition, the Commissioner will continue not to disclose the existence of such a submission for the device for an additional time when any of the following occurs:

(1) The Commissioner requests in writing additional information regarding the device pursuant to § 807.87(g), in which case the Commissioner will not disclose the existence of the submission until 90 days after the Food and Drug Administration's receipt of a complete premarket notification submission;

(2) The Commissioner determines that the device intended to be introduced is a class III device and cannot be marketed without premarket approval or reclassification, in which case the Commissioner will not disclose the existence of the submission unless a petition for reclassification is submitted under section 513(f)(2) of the act and its existence can be disclosed under § 860.5(d) of this chapter; or

(3) The person has requested in the premarket notification submission that the Commissioner protect the confidentiality of the intent to market a device for more than 90 days from the date of receipt of the premarket notification submission by the Food and Drug Administration, and the Commissioner determines that the person has reason to believe that the actual introduction of the device to the market may take longer than 90 days, and the person agrees in a written certification to provide the Commissioner with written notification immediately if the device is put on the market or the intent to market is disclosed. In this case the Commissioner will not disclose the existence of the submission until the Food and Drug Administration's receipt of notification by the person that the device has been put on the market or that the intent to market the device has been disclosed.

(d) Data or information submitted with, or incorporated by reference in, a premarket notification submission (other than safety and effectiveness data that have not been disclosed to the public) shall be available for disclosure by the Food and Drug Administration when the intent to market the device is no longer confidential in accordance with this section, unless exempt from public disclosure in accordance with Part 20 of this chapter. Upon final classification, date and information relating to safety and effectiveness of a device classified in class I (general controls) or class II (performance standards) shall be available for public disclosure. Data and information relating to safety and effectiveness of a device classified in class III (premarket approval) that have not been released to the public shall be retained as confidential unless such data and information become available for release to the public under § 860.5(d) or other provisions of this chapter.

§ 807.97 Misbranding by reference to premarket notification.

Submission of a premarket notification in accordance with this subpart, and a subsequent determination by the Commissioner that the device intended for introduction into commercial distribution is substantially equivalent to a device in commercial distribution before May 28, 1976, or is substantially equivalent to a device introduced into commercial distribution after May 28, 1976, that has subsequently been reclassified into class I or II, does not in any way denote official approval of the device. Any representation that creates an impression of official approval of a device because of complying with the premarket notification regulations is misleading and constitutes misbranding.

510(k) PREAMBLE
(FR 8/23/77)

Final Rule

1.2 **Final Regulation—August 23, 1977**

- 42 FR 42520 -

[Docket No. 76N-0355]

ESTABLISHMENT REGISTRATION AND PREMARKET NOTIFICATION PROCEDURES

AGENCY: Food and Drug Administration.

ACTION: Final rule.

SUMMARY: The agency is issuing final regulations setting forth procedures for the registration of establishments in which devices intended for human use are produced. These regulations also establish requirements governing the form and manner in which premarket notification submissions are to be sent to the Food and Drug Administration (FDA), at least 90 days in advance, by any person who proposes to begin commercial distribution of a device intended for human use in interstate commerce. The Medical Device Amendments of 1976 have provided the agency with the authority to promulgate such regulations to ensure the safety and effectiveness of medical devices for humans. The agency also is establishing rules governing the availability to the public of premarket notification submissions. The existence of a submission and its contents will generally be available to the public upon request, but the regulations provide an exception allowing the existence and contents of certain submissions to be considered confidential commercial information. However, the Commissioner announces his intention to consider further revisions in the regulation when he publishes proposed regulations concerning FDA's handling of public information requests involving new drug applications and related industry submissions to FDA.

EFFECTIVE DATE: September 22, 1977.

(. . .)

SUPPLEMENTARY INFORMATION: The proposed regulations on which these final regulations are based were published in the FEDERAL REGISTER of September 3, 1976 (41 FR 37458). Interested persons were given until November 2, 1976 to comment.

Forty-seven comments were received on the proposal. The issues most often raised by these comments concerned the exemptions from registration, the requirements for submitting a premarket notification when a change or modification is made to a device already on the market, the FDA review of premarket notification submissions, and the confidentiality of premarket notification submissions.

In general, the final regulation has been adopted as proposed, although several changes have been made in response to the comments and to clarify the language of the regulation.

(. . .)

PREMARKET NOTIFICATION PROCEDURES

17. Comments asserted that FDA should not require a premarket notification submission when a person intends to reintroduce into commercial distribution a device that had once been in commercial distribution but had been subsequently discontinued. The comments stated that there is no legal or factual basis for such a requirement. One comment stated that there is nothing in the legislative history of section 510(k) of the act to substantiate the view that a discontinuance of commercial distribution before May 28, 1976, means that the device

should not be considered to have been on the market prior to May 28, 1976. Another comment indicated that the House Report stated that section 510(k) of the act was "designed to insure that manufacturers do not intentionally circumvent the automatic classification of 'new' devices" (Medical Device Amendments of 1976, February 29, 1976, H.R. 94-853 at 37) and argued that this purpose would not be served by requiring a premarket notification submission for the reintroduction of a device on the market prior to May 28, 1976. An additional comment noted that no practical purpose would be served by this requirement since FDA would be notified of the reintroduction of any device under the device listing procedures of section 510(j) of the act.

The Commissioner generally agrees that it is not necessary to require a premarket notification submission for the resumption of commercial distribution of a device that was on the market and was later discontinued by the manufacturer. The owner or operator will, however, be required to report under the device listing regulations the resumption of commercial distribution of a device. The device listing regulations will be published in the FEDERAL REGISTER in the near future.

The owner or operator would not be circumventing the automatic classification of "new" devices if the device had previously been in commercial distribution and had been classified. The Commissioner cautions, however, that if the device in question has been changed or modified to the extent that a premarket notification would be required under the criteria of proposed § 807.81(a)(3), a premarket notification submission would then be required.

18. Numerous comments requested clarification or changes in proposed § 807.81(a)(3) with reference to situations requiring a premarket notification submission when a change or modification is to be made to a device already in commercial distribution. These comments stated that: (1) There is no need to require a premarket notification submission when a proposed change will increase the safety or effectiveness of the device. (2) Not every change in design, material, chemical composition, energy source, and manufacturing process is a significant change affecting the safety or effectiveness of the device and therefore a premarket notification submission should not be required for every such change. Instead, the regulation should identify what types of changes are significant enough to require a premarket notification submission. (3) The Food and Drug Administration should not require a premarket notification submission for every change in manufacturing process since too many such changes are made on a regular basis.

The Commissioner believes that FDA should be aware of and determine whether or not a change will increase the safety or effectiveness of the device. Proposed § 807.81(a)(3)(i), therefore, has been changed in the final regulation to require that a premarket notification be submitted only for changes that could significantly affect safety or effectiveness, whether or not the manufacturer believes that it will increase or decrease safety or effectiveness.

The Commissioner did not intend that the owner or operator should submit a premarket notification for every change in design, material, chemical composition, energy source, or manufacturing process. This list was only intended as an example of some types of changes that often affect safety or effectiveness. The manufacturer is required to submit a premarket notification only if the change could significantly affect the safety or effectiveness of the device, whether or not it is a change of one of the types given as examples. A change has been made in new § 807.81(a)(3) to indicate that premarket notification is required only if the change or modification could significantly affect the safety or effectiveness of the device or if there is a major change or modification in the intended use of the device.

Under the act, the burden is on the manufacturer to determine whether a premarket notification should be submitted for a change or modification in a device. The Commissioner believes that the manufacturer is the person best qualified to make this determination. If appropriate, FDA will notify the manufacturer that the premarket notification that was submitted need not have been submitted so that he may be aware that premarket notification is not required in such a situation. From such experiences, FDA may eventually draw some guidelines as to when a premarket notification submission is not required.

A question has been raised whether a premarket notification is required when a Firm B purchases the product line of a Company A, including the manufacturing facility for that product. The Commissioner believes that a premarket notification would not be required in that situation unless the device has been changed or modified to the extent that the provisions of § 807.81(a)(3) would apply. Section 510(k) of the act would not apply to this situation because Firm B would not be proposing "to begin the introduction or delivery for introduction into interstate commerce for commercial distribution" of a device. Rather, Firm B would be marketing the device in place of Company A.

In such instances, FDA will be notified of a change in ownership by other means. Under new § 807.26, the owner or operator must report a change in individual ownership or corporate or partnership structure within 30 days of the change. The owner or operator will also be required to report a change in ownership under the device-listing procedures to be published as proposed regulations in the FEDERAL REGISTER in the near future.

19. A comment objected that, under proposed § 807.85, the exemption from premarket notification to be granted to custom device manufacturers would not be allowed if the device is offered through advertising by the manufacturer, importer, or distributor. The comment noted that the dissemination of this information is essential to the medical community in obtaining the medical devices needed to treat all patients.

The prohibition of advertising in § 807.85 is intended to apply only to the advertising of a particular device. It does not prohibit the custom device manufacturer from advertising that he manufactures custom devices of a particular generic type. The exemption for manufacturers of custom devices is intended to apply to only those who are customizing devices to fit the needs of a particular patient so that they will not be required to file a premarket notification for each particular device. This reasoning does not apply if the manufacturer, through advertising, is generally offering a particular device for sale. If the device is widely offered through advertising, it could not be considered a custom device.

20. The Commissioner is adding to new § 807.85 exemptions from premarket notification for a distributor who places a device in commercial distribution for the first time under his own name and for a repackager who places his own name on a device, neither of whom otherwise changes the labeling or affects the device. The exemption applies if the device was in commercial distribution before May 28, 1976, the date of enactment of the Medical Device Amendments of 1976, and is being classified. If a premarket notification was submitted by another person, another premarket notification would be a duplication and would not be necessary.

21. One comment suggested that FDA exempt from the premarket notification requirements a device that has been changed by the manufacturer if (1) the device has the intended purpose of only performing in vitro diagnostic tests; (2) the change is intended to improve the device; and (3) the change does not require a change in labeling.

The Commissioner disagrees with the suggestion. A change can be made to an in vitro diagnostic product which does not require a change in labeling but that is significant enough to affect the safety and effectiveness of the device. Premarket notification must be required for such a change.

22. The Commissioner has also added to new § 807.87(a) a requirement that a premarket notification submission contain the classification name of the device, if known. This name is the one used by the classification panels in the classification process under section

513 of the act. Use of the classification name will be discussed further in the preamble to the proposed device-listing regulations, which will be published in the FEDERAL REGISTER in the near future. The Food and Drug Administration will furnish a list of classification names with the device-listing forms or upon request.

The Commissioner has added to new § 807.87(b) a requirement that a premarket notification submission contain the establishment registration number, if any, of the owner or operator submitting the premarket notification. This is to be used to identify registered manufacturers. The Food and Drug Administration will provide any person who does not supply an establishment registration number in the premarket notification with appropriate instructions on establishment registration.

The Commissioner has also added to new § 807.87(e) a requirement that a premarket notification include photographs or engineering drawings where applicable. Photographs or drawings should be submitted when they will aid in understanding the operation of the device.

23. One comment noted that proposed § 807.87(c) (redesignated § 807.87(d)) required that a premarket notification submission contain a statement of the action taken to comply with the premarket approval requirements of section 515 of the act, even though under proposed § 807.81(b) a premarket notification submission is not required when a premarket approval application has been submitted for the device.

The Commissioner agrees with this comment. If a premarket approval application has been submitted, a premarket notification submission would not be required since FDA would already be advised of the intent to market. Accordingly, the requirement has been deleted from the final regulation.

24. One comment objected that under proposed § 807.87 too much information is required to be included in a premarket notification submission. The comment asserted that section 510(k) of the act was intended to require notification only and not "mini-premarket approval."

The requirements of section 510(k) of the act are intended not only to notify FDA that a device is about to be marketed but primarily to enable FDA to determine whether the device is substantially equivalent to one already in commercial distribution. The information required by § 807.87 is necessary to carry out this purpose and is not intended to be a "mini-premarket approval application."

25. Several comments asserted that FDA has no authority for the requirement in proposed § 807.87(d) (redesignated § 807.87(e)) that representative advertisements be included in the premarket notification submission; the comments stated that under section 510(j)(1)(B) of the act, FDA may only require the submission of advertisements for restricted devices. One comment noted that advertisements may not yet be available 90 days before the marketing date.

The limiting procedures of section 510(j)(1)(B) of the act apply only to the listing of devices and therefore do not limit the authority of the Commissioner to require the submission of advertising with premarket notifications under section 510(k) of the act. Section 510(k) provides that premarket notification shall be submitted in such form and manner as the Commissioner shall by regulations prescribe. The Commissioner is of the opinion that this is authority for requiring the submission of representative advertisements. The submission of advertisements is necessary to show the uses for which a device is being promoted so as to determine whether the device is substantially equivalent to a device already in commercial distribution.

26. Several comments addressed proposed § 807.87(e) (redesignated § 807.87(f)) which requires the inclusion of a statement in the premarket notification submission indicating how a device is or is not substantially equivalent to a device already in commercial distribution and data to support that statement. One comment suggested that data to support the statement should be required only if necessary since, in many cases, it will be obvious if a device is substantially equivalent. Three comments suggested that FDA define more clearly the type

of data needed to support a statement that a device is substantially equivalent. Also, one comment stated that it is not appropriate to require that supporting data be included in a premarket notification submission since section 510(k) of the act is a notification provision and not a premarket approval provision.

It has been pointed out above that submission of certain information is necessary to carry out the purpose of section 510(k) of the act. From the information submitted pursuant to section 510(k) of the act, the Commissioner must

be able to determine whether the device is substantially equivalent to one already in commercial distribution. The type of data needed to support a claim that one device is substantially equivalent to another will vary widely depending on the type of device. The Commissioner cannot make a more specific statement as to the type of information required. The information that is necessary must be determined on an individual basis. The manufacturer is best qualified to determine the type of information that should be submitted to demonstrate that his device is substantially equivalent to another device that was on the market on May 28, 1976 or is equivalent to a device that has been classified into class I or II.

The amount of data needed to support a claim of substantial equivalence also will vary widely. In some instances, the data needed to support claims of substantial equivalence will be minimal. The Commissioner therefore rejects the comments suggesting that supporting data only be required if necessary.

27. One comment objected that under proposed § 807.87(g) (redesignated § 807.87(h)), the owner or operator would have to wait an additional 90 days to market the device after submitting a new or amended premarket notification submission, when the Commissioner determines that the original submission was insufficient. The comment asserted that section 510(k) of the act does not provide for the approval or disapproval of a premarket notification submission and also does not contain any provisions that would allow the agency to keep a device off the market more than 90 days after the original filing of the premarket notification submission. One comment suggested that if the additional information requested for a premarket notification submission is submitted within 45 days of the original intended market date, the owner or operator should be allowed to market the device on the original date.

Several comments objected to the basic concept under proposed § 807.87(g) (now § 807.87(h)) that allows the Commissioner to request additional information from the owner or operator when there is insufficient information in the original premarket notification submission to determine whether the device is substantially equivalent to one already in commercial distribution. (Proposed § 807.87(g) also required that the requested information be submitted at least 90 days before the owner or operator intended to market the device.) Five comments noted that the preamble to the proposed regulation stated that the Commissioner would notify the owner or operator within 30 days if the information contained in the premarket notification submission was insufficient, but that no such statement was included in the regulation. Another comment stated that the regulation should require that FDA specify in its notification to the owner or operator exactly what information is lacking in the premarket notification submission.

As noted above, section 510(k) of the act is more than a notification provision. The Commissioner must determine whether the device about to be marketed is substantially equivalent to one already in commercial distribution. To this end, section 510(k) of the act provides that the notification shall be made in such form and manner as the Commissioner shall prescribe. The Commissioner therefore has the authority to reject a notification which does not meet the prescribed form or one which does not contain adequate information.

In most cases, the Commissioner will make any necessary request for additional information within 30 days after the original submission. However, in certain cases, the Commissioner may have to request additional information after the initial 30-day period. The Commissioner must retain this option to ensure that he obtains the information that is necessary to make a proper decision on a premarket notification. Therefore, the Commissioner rejects the comment that suggested that the regulation should require the Commissioner to request any necessary additional information within 30 days after the initial submission.

After the Commissioner requests additional information and the information is submitted, the amended premarket notification will receive expedited review and FDA will generally respond to it in far less than 90 days. However, in certain cases, the additional information may be substantial and a 90-day period may be needed to review this information. The Commissioner therefore rejects any suggestion that FDA should allow the device to be marketed less than 90 days after the submission of the additional information.

If possible, the Commissioner will notify the person submitting the premarket notification of the specific information required to complete the submission. However, in some cases, this may not be possible. The Commissioner believes that the manufacturer is best qualified to show whether his product is substantially equivalent to one already on the market. The Commissioner therefore rejects the suggestion that the regulation require the Commissioner to specify exactly what information is lacking in a premarket notification submission. However, the Commissioner will provide this information to the applicant, where appropriate.

The Commissioner is adding a requirement to new § 807.87(h) stating that, if the additional information is not submitted within 30 days after it is requested, the Commissioner will consider the premarket notification submission to be withdrawn. In such cases, the device cannot be marketed unless (1) a new premarket notification is submitted and the device is declared substantially equivalent, or (2) the device is classified in class I or II pursuant to a petition filed under section 513(f)(2) of the act, or (3) the device is the subject of an approved premarket approval application under section 515 of the act.

28. The Commissioner has revised § 807.95(a) to clarify that in all cases the existence of a premarket notification submission is to be available for public disclosure upon request when a device is marketed or the manufacturer or distributor discloses his intent to market the device. This is true whether any period for confidentiality that FDA granted the notification has expired and whether the premarket notification was submitted before or after the effective date of these regulations.

The proposal did not address the possibility that the person submitting a premarket notification submission might disclose his intent to market the device, nor did the proposal indicate whether FDA would respond to public information requests about whether there had been a submission for an already marketed or advertised product. The agency has no grounds for withholding information that would reveal the intent to market a device when the person submitting the premarket notification submission has revealed these marketing plans, or when marketing has already occurred. There may be instances in which a manufacturer seeks to discover whether a competitor has violated the act, by determining whether there is a premarket notification submission for a device. However, the fact that a manufacturer has not submitted such a notification is not confidential commercial information that is exempt from disclosure, however useful or interesting it might be. Handling of public information requests for premarket notification submissions is facilitated when those requests are accompanied by evidence that there has been public disclosure of the intent to market a device, or that marketing is begun, or when FDA has obtained such evidence from other sources.

The Commissioner also has clarified in § 807.95(c) the duration of confidentiality for premarket notification submissions in the three situations where submissions may be granted confidential treatment for more than 90 days.

Of course, none of these provisions for continued confidentiality apply once the device is marketed or the person who submitted the premarket notification has revealed the intent to market the device.

First, if the Commissioner requests additional information regarding the device under § 807.87(h), the existence of the submissions will not be disclosed until 90 days after the agency's receipt of a complete premarket notification submission.

Second, if the Commissioner determines that the device is a class III device, it cannot be marketed without premarket approval or reclassification. When the Commissioner makes this determination, the existence of the submission will not be disclosed unless a petition for reclassification is submitted under section 513(f) of the act and its existence can be disclosed under proposed § 860.5(d). Proposed § 860.5(d) is a provision of the agency's classification regulations to be published in the FEDERAL REGISTER in the near future, and is consistent with the requirements in section 513(f)(2) of the act that FDA provide opportunity for public participation in reclassification of new devices and in section 520(c) of the act that FDA not rely on trade secrets or other confidential commercial information as the basis for reclassifying a class III device. Future FDA regulations will address the confidentiality of intent to market a device when an application for premarket approval of a device is submitted under section 515 of the act. The Commissioner believes that it will be very unlikely that the intent to market a device that is the subject of such an application would in fact be confidential, because the sponsor would almost invariably have had to reveal its marketing plans to some persons outside the company and because of the statutory requirement for advisory committee review.

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Third, if the person requests, and FDA agrees, that the intent to market a device be held in confidence for more than 90 days because the person has reason to believe that the actual marketing of the device may be delayed, the Commissioner will not disclose the existence of the submission until FDA receives the required notification that the device has been put on the market or that the intent to market the device has been disclosed.

Once FDA can disclose the fact that a premarket notification submission exists, the contents of the submission (other than information protected under § 807.95(d)) will be available for public disclosure.

29. Several comments asserted that the intent to market a device should be kept confidential without the owner or operator having to request confidentiality as required by proposed § 807.95(a). The Commissioner believes that it is appropriate to require the person submitting the premarket notification submission to request that it be kept confidential. The intent to market a device will in many cases be known to persons outside the company, and the Commissioner believes that information concerning a premarket notification submission, including its existence, should be available for public disclosure, upon request, unless the person submitting it shows that the intent to market the device is confidential commercial information.

The Commissioner has revised § 807.95 to require a person submitting a certification of confidentiality to include a statement that the person understands that the submission to the government of false information is prohibited by 18 U.S.C. 1001 and 21 U.S.C. 331(q). This change underlies the importance of submitting truthful requests for confidential treatment of premarket notification submissions and thus discourages indiscriminate claims of confidentiality. The Commissioner also is requiring the person submitting the request for confidentiality to agree to notify FDA immediately if the person discloses the intent to market the device to anyone, except employees of or paid consultants to the establishment, or individuals in an advertising or law firm pursuant to commercial arrangements with appropriate safeguards for confidentiality.

30. Another comment stated that the intent to market a device should be kept confidential until the owner or operator notifies FDA of the actual marketing of the device.

The regulations have retained the provision that the existence of the premarket notification submission, and thus the contents other than trade secrets, will be kept confidential for 90 days when the person submitting it demonstrates to the agency's satisfaction that the intent to market the device is confidential. The agency believes this approach is more workable in most cases than that suggested by the comment. However, under § 807.95(b)(1)(iii) the Commissioner will keep the intent to market a device confidential until actual marketing of the device begins when this is expected to occur more than 90 days after the premarket notification if the person submitting it convinces FDA that the notification should be kept confidential until actual marketing begins and agrees to comply with certain specified conditions, including a requirement to notify the Commissioner when the device is marketed or when the person reveals the intent to market the device.

31. Other comments opposed the conditions placed on persons seeking to protect the confidentiality of a premarket notification submission. Several comments objected to the fact that proposed § 807.95 required the owner or operator to certify that he has not released the information to individuals outside the company who are not paid consultants. These comments pointed out that the owner or operator may have to release the information to investigators and scientists who are not paid. The comments also stated that the intent to market a device should be kept confidential by FDA if the intent to market is made known to individuals not in the employ of the owner or operator but who are in a confidential relationship with him and if the manufacturer has taken reasonable steps to protect the confidentiality of the information. One comment stated that the intent to market a device may necessarily be released on a confidential basis to advertising personnel and others who do not fall within the category of employees of the establishment under proposed § 807.95(a)(1) but should nevertheless be kept confidential.

The Commissioner agrees that a discussion with individuals in an advertising firm or a law firm should not be regarded as a breach of confidentiality of the intent to market a device and has revised the regulation accordingly.

32. One comment stated that material dealing with comparative literature and data to support a claim of substantial equivalence should be exempt from disclosure because it could be relevant in the event there is litigation involving patent infringement.

Under § 807.95(d), data and information submitted pursuant to the premarket notification regulations that are trade secret information shall be held as confidential. The Commissioner cannot, however, make a broad statement that all material dealing with comparative literature and data to support substantial equivalence will be considered confidential. The possibility that such information could be relevant in litigation involving patent infringement does not provide FDA with grounds for withholding the information under any exemption to the Freedom of Information Act. Although evidence that a competitor infringed a patent may be commercially useful information, it is not confidential commercial information that is entitled to confidentiality. The Commissioner notes, however, that a determination of substantial equivalence under the Federal Food, Drug, and Cosmetic Act relates to the fact that the product can lawfully be marketed without premarket approval or reclassification. This determination is not intended to have any bearing whatever on the resolution of patent infringement suits.

33. The Commissioner cautions that FDA may in the future propose revisions in the policy set forth in § 807.95. FDA currently is reviewing the procedures by which it handles requests for disclosure of information concerning the existence of a variety of submissions that are made to it, including new drug applications, new animal drug applications, and device premarket approval applications. The agency may revise its current procedures so as to acknowledge in all cases the existence of these pending submissions. Because the proper method of handling requests for data and information on device premarket notification submis-

sions involves many of the same issues that are involved in requests for information on new drug applications and similar applications, § 807.95 may eventually be revised in future regulations in light of the agency's decisions on how all such related submissions should be handled.

The Commissioner has had to decide how to handle public information requests for premarket notification submissions received before the effective date of these regulations. Freedom of information requests have been received for such premarket notification submissions review by FDA. There is no question about the agency's handling of these requests where FDA knows, either from the public information requests or from other sources, that the device has been put on the market or the intent to do so has been disclosed: The existence of the notification and its contents, other than any bona fide trade secrets, are disclosable. More difficult questions arise in situations in which FDA simply does not know whether a device that was the subject of a submission has been put on the market or the intent to do so has been disclosed. Therefore, as discussed below, FDA is requiring, by October 24, 1977, submission of justification for continued confidential treatment for most premarket approval notifications received before the effective date of the regulation.

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The following describes how FDA is dealing with requests concerning premarket notification submissions received before September 22, 1977, the effective date of the regulations:

a. The existence of the premarket notification submission and its contents, other than bona fide trade secrets, shall be available for public disclosure if the device has been marketed or if the intent to market the device has been disclosed.

b. During the 90 days after the submission of a premarket notification submission, FDA will treat the existence of the submission and its contents as confidential unless the agency has information that the device has been marketed or the intent to market the device has been disclosed.

c. If the submission indicated that marketing was not expected for more than 90 days, and requested confidential treatment until marketing began, and included an agreement to notify FDA when marketing began, FDA will treat the existence of the submission and its contents as confidential unless the agency has information that the device has been marketed or the intent to do so has been disclosed. If much time has elapsed since the expiration of the 90-day notification period, FDA will make reasonable efforts to determine whether a device which was the subject of a submission has been put on the market or the intent to market the device has been disclosed.

d. Any premarket notification submission received before the effective date of the regulations shall be available for public disclosure 90 days after its receipt by FDA except to the extent that the person who submitted the submission demonstrates by October 24, 1977, that the existence of the submission and its contents are still entitled to confidentiality. Where the FDA receives a public information request for a submission more than 90 days after the submission's receipt, but before October 24, 1977, FDA will make reasonable efforts to determine whether the device has been put on the market or the intent to market the device has been disclosed. A person who seeks to demonstrate that the existence of a submission is still confidential should submit the necessary documentation to the Food and Drug Administration, Bureau of Medical Devices (HFK-20), 8757 Georgia Ave., Silver Spring, Md. 20910. This documentation should indicate whether the device has not been marketed or the intent to do so has not been disclosed except to employees of or paid consultants to the establishment, or to individuals in an advertising or law firm pursuant to commercial arrangements with appropriate safeguards for secrecy.

e. Where a public information request is made concerning a premarket notification submission and there is no submission or there is a submission whose existence is confidential under b, c, or d above, FDA will respond to the request by indicating that no submission described in the request has been received that is disclosable, and that FDA cannot indicate whether a submission has been received.

f. To determine whether the intent to market a device has been disclosed, FDA is applying the rules in § 807.95.

PREMARKET NOTIFICATION REVIEW PROGRAM

The following guidance document on CDRH's Premarket Notification review program outlines the requirements for premarket notification review, discusses some general points FDA normally considers when deciding if a device is "substantially equivalent," and presents a list of criteria and two flowcharts depicting a condensed version of the 510(k) process.

This guidance document describes practices that have developed over many years of program operations, and that have been refined as a result of several years of internal CDRH discussions that included input from the Center's device evaluation staff. This document was originally intended for use by 510(k) reviewers and given the complexity of the 510(k) program may need refinement or expansion over time.

GUIDANCE ON THE CENTER FOR DEVICES AND RADIOLOGICAL HEALTH'S PREMARKET NOTIFICATION REVIEW PROGRAM

(June 30, 1986)

Purpose of the Guidance

This guidance document outlines requirements for premarket notification review, and explains some points the Center for Devices and Radiological Health (CDRH) will consider when making a determination that a device is, or is not, "substantially equivalent." A consistent application of the principles set forth in the guidance should be useful to Center staff in conducting complete and expeditious reviews of 510(k) submissions.

Purpose of the Program

In brief, the premarket notification program is meant to:

- o identify new devices that must be placed automatically into Class III and undergo premarket approval or reclassification before they are marketed;
- o classify new devices; a not substantially equivalent (NSE) new device is in Class III, and a substantially equivalent (SE) new device is in the same regulatory class as the device to which it is found equivalent; and
- o achieve marketing equity by allowing manufacturers of new devices that are SE to preamendments devices to market their devices without facing any greater regulatory burdens than faced by manufacturers of the preamendments devices.

Background

The Statute: The Medical Device Amendments were enacted on May 28, 1976. They direct FDA to issue regulations that classify all devices that were in commercial distribution at that time into one of three regulatory control categories, Class I, II, or III, depending upon the degree of regulation necessary to provide reasonable assurance of their safety and effectiveness. The class into which a device is placed determines the requirements that must be met before a manufacturer may distribute the device in interstate commerce.

Class I devices are subject to a comprehensive set of regulatory authorities applicable to all classes of devices; e.g., premarket notification, registration and listing, prohibitions against adulteration and misbranding, and rules for good manufacturing practices. Class II devices also need performance standards, and Class III devices need premarket approval.

The Federal Food, Drug, and Cosmetic Act (Act) also specifies how a new device; i.e., a postamendments device, is to be classified. A postamendments device is automatically in Class III and must undergo premarket approval or reclassification before it can be marketed, unless it is within a type of device that was in commercial distribution prior to May 28, 1976 and is SE to another device within such type; or, it is within a type of device introduced after May 28, 1976 that has been reclassified into Class I or II and is SE to another device within such type. An SE device is in the same class and is subject to the same requirements as the device to which it is SE.

Section 510(k) of the Act requires a person who wishes to introduce a device into commerce to notify the Center at least ninety days in advance. This premarket notification is referred to as a "510(k)." The Agency uses 510(k)s to determine if new devices are, or are not, SE to either a preamendments device or a reclassified postamendments device.

Congressional Guidance: The statutory objectives for the 510(k) program are clear. Also, the Report by the Committee on Interstate and Foreign Commerce on the Medical Device Amendments of 1976 (House Report) offers some additional guidance on program implementation, describing the term "substantial equivalence" as follows:

> The term "substantially equivalent" is not intended to be so narrow as to refer only to devices that are identical to marketed devices nor so broad as to refer to devices which are intended to be used for the same purposes as marketed products. The committee believes that the term should be construed narrowly where necessary to assure the safety and effectiveness of a device but not narrowly where differences between a new device and a marketed device do not relate to safety and effectiveness. Thus, differences between "new" and marketed devices in materials, design, or energy source, for example, would have a bearing on the adequacy of information as to a new device's safety and effectiveness, and such devices should be automatically classified into Class III. On the other hand, copies of devices marketed prior to enactment, or devices whose variations are immaterial to safety and effectiveness would not necessarily fall under the automatic classification scheme. 1/

If substantial equivalence were judged too narrowly, the marketing of devices that would benefit the public would be delayed; the device industry would be unnecessarily exposed to the greater burdens of premarket approval; new devices would not be properly classified; and new manufacturers of preamendments type devices would not have marketing equity. If substantial equivalence were judged too broadly, the statutory purpose may not be served; i.e., devices with new uses or those presenting new or different risks would be marketed without adequate regulatory control.

The 510(k) Regulation: On August 23, 1977, FDA issued a final regulation for Establishment Registration and Device Listing for Manufacturers of Devices (21 CFR Part 807). Subpart E describes premarket notification procedures. The 510(k) rules were incorporated into the registration and listing regulation because the 510(k) requirements apply only to those persons required to register.

The regulation describes the circumstances under which a 510(k) must be submitted, the information required, and the FDA rules for maintaining confidentiality of submitted information. Essentially, the regulation provides that a person required to register must submit a 510(k) at least ninety days before marketing a device that:

o is being introduced into distribution for the first time by that person, or

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1/ H.R. Rep. No. 94-853, pp. 36-37. The Amendments, as enacted, are comprised primarily of the bill H.R. 11124 as drafted by the Subcommittee on Health and the Environment of the Committee on Interstate and Foreign Commerce and adopted by the House of Representatives. This report provides the only Congressional guidance on the criteria for substantial equivalence.

- is in distribution but is being significantly modified in design. use. etc. 2/

A 510(k) must contain. among other things:

- proposed labeling sufficient to describe the device's intended use:
- a description of how the device is similar to or different from other devices of comparable type. or information about what consequences a proposed device modification may have on the device's safety and effectiveness: and
- any other information the Center needs to determine whether the device is SE.

The statute provides that a new device can be SE to one of two types of devices (from hereon referred to as a "predicate device"). A predicate device is one that was in distribution prior to enactment of the Amendments. or it is a postamendments device that was subject to reclassification from Class III to Class I or II. The Center does not routinely require that manufacturers perform research to determine what specific predicate devices were available in 1976. or were available at the time a postamendments device was reclassified from Class III to Class I or II: nor does the Center routinely require that all 510(k)s initially provide information on a predicate device. Instead. the Center requires submitters to provide information that compares the new device to a marketed device of a similar type. regardless of whether this marketed device was marketed before or after enactment of the Amendments. or before or after a type of postamendments device was reclassified.

This means that the manufacturer can submit a 510(k) comparing a new device to a device that has been found to be SE. It does not mean. however. that the Center finds new devices SE to devices that have been found SE. It only reflects the agency's position that the similarity of a new device to a marketed device is evidence that can be considered in determining that the new device is. as is the marketed device to which it is compared. SE to a predicate device. Nevertheless. the ultimate burden of demonstrating the substantial equivalence of a new device to a predicate device remains with the 510(k) submitter. and in those occasions when the Center is unfamiliar with certain aspects of the predicate device. the submitter will be required to provide information that substantiates a claim of substantial equivalence.

The guidance that follows assumes that 510(k)s provide comparisons with marketed devices.

General Points Considered by CDRH During the Review of 510(k) Submissions

CDRH normally approaches the review of 510(k)s by considering the following points:

- Does the new device have the same intended use as a predicate device?
- Does the new device have the same technological characteristics: i.e.. same materials. design. energy source. etc.?

2/ This document does not provide guidance on what changes in marketed devices are significant enough to require the submission of a 510(k). but the Center plans to issue such guidance in the near future.

- o If it has new technological characteristics, could they affect safety or effectiveness?

If the new device has a new intended use (what constitutes a new intended use is discussed below), it is considered NSE. If the new device has the same intended use as a predicate device and the same technological characteristics related to safety and effectiveness, the new device is considered SE. If the new device has the same intended use as a predicate device, and it has new technological features that could affect safety or effectiveness, additional issues are considered:

- o Do the new technological features pose the same type of questions about safety or effectiveness as are posed by the predicate device with the same intended use?
- o Are there accepted scientific methods for evaluating whether safety or effectiveness has been adversely affected as a result of the use of new technological characteristics?
- o Is there information to demonstrate that the new technological features have not diminished safety and effectiveness?

If the answers to any of the above questions are negative, the device is generally considered NSE.

Thus, as a matter of practice, CDRH generally considers a device to be SE to a predicate device if, in comparison to the predicate device:

- o the new device has the same intended use (as discussed below); and
- o the new device has the same technological characteristics (i.e., same materials, design, energy source, etc.); or, it has new technological characteristics that could not affect safety or effectiveness; or
- o it has new technological characteristics that could affect safety or effectiveness, and
  - it generates the same type of questions about safety or effectiveness;
  - there are accepted scientific methods for evaluating whether safety or effectiveness has been adversely affected as a result of the use of new technological characteristics; and
  - there are data to demonstrate that the new technological features have not diminished safety or effectiveness. 3/

Premarket notification submissions should be designed to answer these questions. The guidance below describes how the Center draws conclusions about the questions. The guidance covers the meaning of "intended use," technological changes that can be reviewed under the 510(k) process, data that are required in a 510(k), and what "combination" devices can be 510(k)'ed. Also, the attached flow charts illustrate the decision making process.

3/ See attached list of criteria for substantially equivalency.

The Meaning of Intended Use

While a new device must have the same intended use as a predicate device in order to be SE, the Center does not require that a new device be labeled with precise therapeutic or diagnostic statements identical to those that appear on predicate device labeling in order for the new device to have the same intended use. Label statements may vary. Certain elements of a predicate device's labeled indication may not be critical to its intended therapeutic, diagnostic, prosthetic, surgical, etc., use. The Center's scientific expertise enables it to exercise considerable discretion in construing intended uses in the labeling and promotional materials for predicate and new devices. 4/ Thus, a new device with the same intended use as a predicate device may have different specific indication statements, and as long as these label indications do not introduce questions about safety or effectiveness different from those that were posed by the predicate device's intended use, the new device may be found SE.

For the purposes of determining whether or not the new device has the same intended use as a predicate device, the Center assesses any differences in label indications in terms of the safety and effectiveness questions they may raise. The Center considers such points as physiological purpose (e.g., removes water from blood, transports blood, cuts tissue), condition or disease to be treated or diagnosed, professional or lay use, parts of the body or types of tissue involved, frequency of use, etc. If a new device is determined to have the same intended use, the Center may then proceed to determine whether or not it is substantially equivalent. (Devices which do not have the same intended use cannot be substantially equivalent.) The following examples illustrate these concepts.

> **Nonimplanted blood access device:** This type of preamendments Class II device is intended to provide access to a patient's blood so that blood can, for example, be subjected to hemodialysis. Pre-1976 devices are labeled for insertion into the femoral vein. New devices that are labeled for insertion into the subclavian vein may have the same intended use to the extent that labeling for the new and predicate devices indicates that both are intended to provide access to a patient's blood for similar purposes. The differences in labeling described above do not undercut the fact that the new and predicate devices have the same intended use. CDRH was further able to conclude that, because the differences in labeling related only to a method of use not relevant to the effect that the insertion is to achieve (and therefore did not pose new safety or effectiveness questions) and because there were no other significant changes (in technology, design, etc.), the new device was substantially equivalent.
>
> **Conventional dialyzer:** This type of preamendments device is in Class II. The preamendments devices are labeled for use as part of an artificial kidney system for patients with renal failure. The principal purpose of the device is to remove excess water from the vascular system. Some new devices that have been found SE are labeled for use as part of a heart-lung machine to remove excess water from the vascular system at the end of surgery. Again, the Center concluded that this is not a different intended use. Differences in the labeling relate only to a nonessential condition that does not bear materially on the safe and effective use of the device, and moreover, there are no other significant changes (in technology, design, etc.); therefore, the devices are substantially equivalent.

4/ Ordinarily, intended use is determined by reference to "labeling" or promotional claims; only in rare cases might it be necessary to infer intended use from other types of information.

Blood tubing set: This preamendments Class II device consists of tubing that enables blood to flow from a patient to a dialyzer and back to the patient. Some new devices that have been found SE are labeled for use in carrying blood to and from a plasmapheresis device. The Center concluded that this is not a different use for the two tubings.

The labeling differences relating to the subclavian catheter, the conventional dialyzer for use with the heart-lung machine, and the blood tubing set for plasmapheresis, are not significant enough to require a finding that the devices are for different intended uses. Moreover, the specific uses associated with the labeling modifications do not present issues of safety and effectiveness different from those posed by the use of their predicate devices, and therefore, the devices can be found SE in terms of intended use. On the other hand, for some new devices, modifications in label indications will not be found to represent the same intended use as a predicate device, even though the intended effect of the new device is very similar to that of the predicate device. This is because slight modifications in intended use can be significant to the claimed effect or purpose of the predicate device. If a device has a different intended use, there is no reason to proceed further to decide whether the devices are substantially equivalent. (Obviously, however, some of the same issues relevant to substantial equivalence determinations may arise in assessing whether or not devices are for the same intended use, i.e., differences in labeling are judged in terms of any safety and effectiveness questions they may raise.) Two examples follow:

Long-term percutaneous intravascular catheter: This preamendments, unclassified device consists of a slender tube labeled for insertion into the vascular system for extended periods in order to sample blood, monitor blood pressure, or administer drugs. A similarly designed device has been found NSE because it is labeled for use as a spinal canal access catheter. The new device was intended to deliver drugs over an extended period of time to the spinal canal. While both devices deliver drugs into the human body, each device relates to a different body system. The concern raised by this difference led to the conclusion that the intended uses of the devices are not the same. Inserting the device into, and maintaining it in, the spinal canal raises significantly different safety issues compared to the issues posed by intravascular insertion; namely, the new device potentially posed risks to the spinal cord, whereas the predicate device did not.

Powered aspirators: These preamendments devices, currently proposed for Class II, were labeled to remove loose bone chips, blood, or tissue from the body during surgery. Similarly designed new devices have been found NSE when labeled for use in "suction lipectomy." In this new surgical procedure, the aspirating device is inserted under the skin to remove body fat, sometimes very large amounts of body fat, for cosmetic purposes. In suction lipectomy, the aspiration process performed by the device becomes the surgical procedure. It is no longer an aspirator merely used as an aid in performing another surgical procedure that is not aimed solely at the removal of fat. For these reasons, the new devices, as labeled, do not have the same intended uses as the predicate device. The difference in intended use is underscored by the fact that removal of large amounts of body fat through aspiration raises questions of safety and effectiveness not posed by the labeled use of preamendments aspirators, e.g., possible metabolic changes, and permanent bagging of the skin resulting when the fat removed from the area exceeds the ability of the skin to contract. Thus, the intended uses are not the same.

As the examples above illustrate, for a device to be found SE, it is important that a 510(k) for the device demonstrate that the intended use of the device does not differ from the intended use of marketed devices within the same type and that any changes in labeling are immaterial in terms of safety and effectiveness issues.

Devices with New Technological Features

If a new device has the same intended use as a predicate device, and there are no technological differences between the new and a predicate device, the new device is SE. If the device has the same intended use and technological differences, but the technological differences could not affect safety or effectiveness, it is SE. If the device has the same intended use and technological differences that could affect safety or effectiveness, the new device may not be SE. Technological differences may include modifications in design, materials, or energy sources; for example, changes in the power levels of electrical surgical instruments, the use of new reagents in **in vitro** diagnostic devices, the use of new materials in orthopedic implants, and the use of new battery designs in implanted pacemakers. The Center finds devices with new technological features to be NSE when the new feature could adversely affect safety or effectiveness in a way that is consequential under the conditions of intended use.

In taking this approach, the Center focuses on the technological differences that are medically and scientifically significant and avoids the difficulties that would arise from a mechanistic application of rigid formal criteria to the wide variety of substantial equivalence questions posed by new devices proposed for marketing under a 510(k). Substantial equivalence determinations of necessity require the Center to exercise reasonable scientific judgment. For example, the strict application of a rule that would make devices NSE if they have a new material would be inappropriate for such devices as bed pans. For other devices, a "materials rule" may seem more appropriate, e.g., for implants. Even for implants, however, such a rule would be too encompassing if applied to substitute materials known to be, or easily shown to be, equivalent or superior; for example, if applied to a new postamendments hip made of titanium, which is generally known to be, and can easily be shown to be, stronger and less corrosive than some stainless steel that was used in preamendments hips.

Thus, from a scientific perspective, to determine which technological changes are consequential, the Center considers whether:

- o the new device poses the same type of questions about safety or effectiveness as a predicate device;
- o there are accepted scientific methods for evaluating whether safety or effectiveness has been adversely affected as a result of the use of new technological characteristics; and
- o there are data to demonstrate that new technological characteristics have not diminished safety or effectiveness.

The examples below should help clarify these concepts.

Electrocardiographs: This device is in Class II. Preamendments electrocardiographs produce an analog visual display of the electrical signals produced by the heart. Some postamendments devices that have been found SE display these signals in a digital, rather than analog form. This technological innovation could affect the effectiveness of the device; i.e., the electronic components used to produce the digital display might not achieve the accuracy of an analog display. The Center found the new devices SE because the modification presented the same questions of effectiveness as posed by the predicate device; i.e., does the display accurately represent the electrical activity of the heart. Also, there are accepted bench test procedures to demonstrate comparability of accuracy between the new and predicate devices, and the necessary comparability information was presented in the 510(k).

Inflatable penile implant: This device is in Class III. The preamendments implants consist of inflatable cylinders implanted in the penis connected to a reservoir filled with fluid and implanted in the abdomen, and a subcutaneous manual pump implanted in the scrotum. When the cylinders are inflated, they provide rigidity to the penis. The connections between the various parts of this system sometimes leaked. Manufacturers of postamendments versions of these devices modified the connector designs. These new devices have been found SE even though such a change could affect safety and effectiveness. This is because the new connectors presented the same questions of safety and effectiveness as posed by the predicate device; i.e., are the connector materials nontoxic and do the connectors leak? Since the materials were the same, questions about the comparability of toxicity were obviated, and bench testing and clinical evidence easily and clearly demonstrated that the modified connectors were not more prone to leaks than the connectors in the predicate devices.

Perimeter: This device is proposed for classification in Class I or II, depending on whether it is manually or electrically operated. The preamendments devices are ac-powered or manual devices that project light on various points of a curved surface, and the patient manually indicates whether he or she sees the light. The devices are designed to determine the extent of a patient's peripheral vision. Manufacturers of postamendments devices have incorporated software into the device. The software automatically lights various points on the curved surface, and keeps track of whether the patient indicates that the light has been seen by recording that the patient has or has not pressed a button. The new device posed the same safety and effectiveness questions as the predicate devices, i.e., are the light-points in the appropriate places, is there risk of shock, do the points light up when they are meant to, and can the patient's reaction be accurately recorded. Because the questions are the same, and obviously accepted testing procedures can ensure comparability of performance between the new and predicate device, and because clinical data showed comparability, the new devices with a software package were found to be SE.

Hemodialyzers: This is a Class II device that is used as an artificial kidney system. The device allows the removal of water and waste from the patient's blood through a semipermeable membrane. Preamendments devices used cellulose based semipermeable membranes. Manufacturers of postamendments devices have used various other types of membranes in the filters and these devices have been found SE. This is because the new membranes raised the same questions of safety and effectiveness as the cellulose membrane, e.g., is the degree of permeability acceptable, is the material toxic, and is the degree of particulate contamination acceptable? Accepted preclinical tests, with clinical confirmation, demonstrated that the new membranes and the cellulose membranes were comparable.

On the other hand, there will be many technological changes that will make a device NSE. For example:

Heart valves: This preamendments type device is in Class III. It is intended to perform the function of any of the heart's natural valves. It is constructed of prosthetic or biological materials, or both. The Center has found many new valves to be NSE even though the new valves, in some cases, incorporated only very slight design modifications in relation to predicate valves. This is not because the device is a high risk device. Rather, it is because of the nature of the device. A minor change in design can raise questions about safety and effectiveness that are inappropriate for evaluation under 510(k). Specifically, different valve designs can lead to a different balance in the performance factors related to valves. Minor changes in a valve may make it more susceptible to fractures than its predicate, but less susceptible to occlusion. In this case, it is difficult to compare the performance of one valve to another because they present different questions about safety; each valve tends to present different risk/benefit equations. As a result, there are no accepted methods for assessing comparability. Consequently, these devices are typically found NSE.

Electrohydraulic lithotripter: This preamendments device is in Class III. The preamendments device was used to fragment urinary bladder stones. It consists of a high voltage cable connected to a bipolar electrode introduced into the bladder through a cystoscope. The Center found an electrohydraulic lithotripter inserted into the ureter through a cystoscope for use on ureteral stones to be SE. The principle of operation for both devices are identical. The stone is fragmented by the discharge of electricity between the two electrical poles. Another postamendments device, known as the Extracorporeal Shock Wave Lithotripter was NSE. This device breaks kidney stones through the use of a succession of externally generated shock waves focused on the stone. The shock waves are transmitted through water in which the patient is sitting, and then transmitted through body tissue to the stone. The device raised questions about safety and effectiveness not present in the previous devices, e.g., the shock waves, which enter large portions of the body, could affect cardiopulmonary functions or could have had unknown effects on much of the tissue and organs in the abdomen. An evaluation of these questions was not appropriate for a 510(k) because they presented issues outside the questions of safety and effectiveness raised by the electrohydraulic lithotripter.

Femoral stem: This lower portion of a total artificial hip replacement is a preamendments device proposed for Class II. Some of these devices are uncemented and are fixed by impaction of the stem into the top of the femur. The preamendments impact/fit stems had smooth, straight (uncontoured) surfaces on the stem that fit into the femur. The Center found SE some postamendments versions of the stem that have surface variations, i.e., grooves, irregular or regular contours, etc., that allow the bone to remodel over time. The Center found to be NSE postamendment stems with porous coatings (for uncemented use) that require bone ingrowth into the device for fixation. The contoured stem relied on impact placement and bone remodeling to an essentially smooth surface. The health of the bone would still depend upon normal bone vascularization systems even if the bone conformed to some of the slightly wavy contours. The questions of safety and effectiveness were the same as those for the traditional impact fit stem. On the other hand, for bone to grow into and remain viable in a porous material, the bone would need to depend upon an intricate vascularization system not normally occurring in bone that may not, in fact, develop or be sustainable. Thus, the porous coated device was found NSE because it presented new scientific questions about long term fixation.

As the examples above illustrate, for a device to be found SE, it is important that a 510(k) for the device either demonstrate that the technology of the device does not differ from the technology of marketed devices within the same type; or, to the extent that the technology does differ, explain why the device does not present new questions about safety or effectiveness, describe what accepted methods exist to test comparability of performance, and present data, generated from such tests, that demonstrate comparability. (See the 510(k) data discussion below. 510(k)s for new devices that are different from predicate devices, but are not different from a marketed device within the same type, may not need to provide testing information.)

Data Requirements For 510(k)s

The requirements of section 510(k) of the Act are intended not only to notify FDA that a device is about to be marketed but primarily to enable FDA to determine whether the device is SE to one already in commercial distribution. To fulfill this responsibility, the Center requires that a 510(k) include **descriptive data** needed to understand a new device's intended use, physical composition, method of operation, specifications, performance claims, etc. Similar information about the device to which the new device is being compared may also be required. In addition, under certain circumstances, the Center requires **performance testing information,** i.e., data from bench, animal, or clinical tests, in order to determine that a device performs according to its description.

While the Center has concluded that it should sometimes require performance testing data in order to confirm that a new device is SE, the 510(k) review process is not a substitute for premarket approval, and the Center does not attempt to address all of the issues that would be answered in a PMA in its review of 510(k)s. Data in a 510(k) should show **comparability** of a new device to a predicate device, whereas demonstration, in an absolute sense, of a device's safety and effectiveness, is reserved for PMAs.

Although there are no hard and fast rules governing all the possible data collection issues that can arise in 510(k)s, the following guidance will govern many situations.

The Center will always require descriptive data necessary to understand a new device's intended use, physical composition, method of operation, specifications, performance claims, etc. Also, the Center will always require any descriptive data necessary to understand the same characteristics of the device to which the new device is being compared.

The Center normally will not require performance testing data to substantiate equivalence if a new device does not have an important descriptive difference in comparison to marketed devices within its type, i.e., it does not have a new material, method of operation, etc., and it has descriptive characteristics that are precise enough to ensure that comparability will be achieved if the new device is manufactured according to its description. For example, the Center will accept the descriptive statement that a new surgical instrument will be made of surgical grade stainless steel, as are other marketed surgical instruments, as substantiation that the new instrument is equivalent in materials/composition to a predicate device. (See below for an explanation of how a comparison to any marketed device can lead to a conclusion about the substantial equivalence of a new device to a predicate device.)

The Center normally will require performance testing data to substantiate equivalence if a new device has an important descriptive difference in comparison to marketed devices within its type, and it is **not** clear from an initial review that the device has an intended use or technological change that makes it NSE; or, the new device has descriptive characteristics that are too imprecise to guarantee that comparability in performance will be achieved even if the new device is produced as described. Following is an example of when descriptive similarities are inadequate to ensure that comparability of performance will be achieved when a new device has the same descriptive characteristics as a marketed device. The fact that a new pacemaker lead and a marketed pacemaker lead are both in the polyurethane "family" does not ensure that both devices have the same chemical formulations, and differences in the chemical formulations of polyurethanes could affect safety or effectiveness. Differences in design, extrusion, and assembly of polyurethanes with the same chemical formulation could also affect safety or effectiveness. Thus, the Center would generally require performance testing information to confirm that the new lead is SE to the predicate lead.

If it is clear from an initial review that a new device has an intended use or technological feature that makes it NSE, the Center will not review or require performance information in the 510(k). Instead, the applicant will be notified that the device is NSE, and any performance data will be reviewed in a PMA or reclassification petition.

Typically, a 510(k) provides descriptive and testing data that compares the new device to another marketed device within the type, but does not necessarily compare the new device directly to a predicate device. In these cases, the Center can rely, as necessary, on performance data appearing in previously reviewed 510(k) files, in Center classification files, or in the literature, to determine that the device is not only comparable to another marketed device within its type, but is also SE to a predicate device.

Nevertheless, the ultimate burden of demonstrating the substantial equivalence of a new device to a predicate device remains with the 510(k) submitter, and in circumstances when the Center is unfamiliar with certain aspects of the predicate device, the submitter will be required to provide information that substantiates a claim of substantial equivalence.

New Devices That are Combinations of Old Devices

A new device is a so-called "combination" device when it claims to have the same intended uses as two or more different types of predicate devices. Normally, this is achieved by combining two or more predicate devices into a device that is sold as a unit, e.g., a urinary catheter may incorporate a temperature measuring device; or a cardiac monitor, electrocardiograph, and blood pressure computer that were sold separately prior to May 28, 1976, might be combined into one electronic monitoring device.

When a new device combines types of devices from different classes, questions have arisen about what classification the new device will have.

In its review of the 510(k), the Center will subject the combination device to the same sorts of questions and documentation requirements that are applied to a single device. When such a device is found to be SE, it combines devices from different classes and is classified in the highest of the predicate device classifications unless the combined devices are regulatable as separate articles, e.g., they are detachable. In that case, the separately regulatable articles will be regulated in separate classes.

Attachment I

CRITERIA FOR SUBSTANTIAL EQUIVALENCE

NEW DEVICE IS SUBSTANTIALLY EQUIVALENT IF, IN COMPARISON TO A PREDICATE DEVICE, IT:

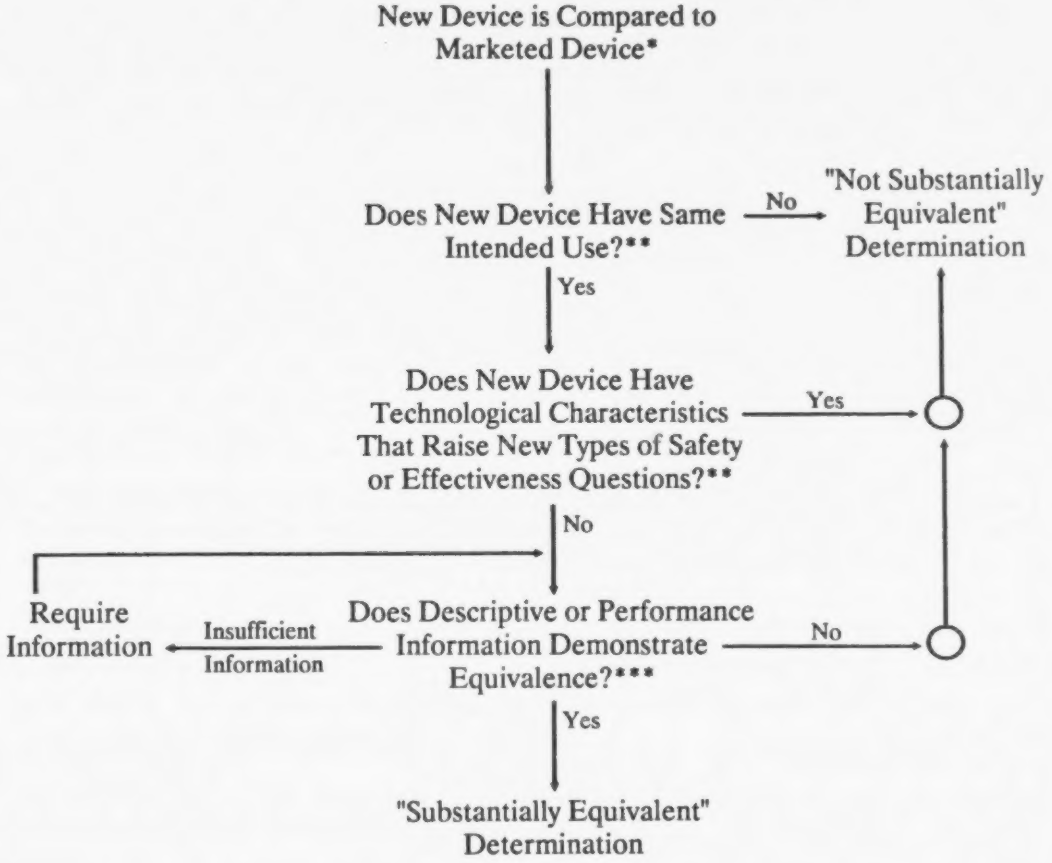
- HAS SAME INTENDED USE; AND

- HAS SAME TECHNOLOGICAL FEATURES OR NEW FEATURES THAT DO NOT AFFECT SAFETY OR EFFECTIVENESS; OR

- HAS NEW TECHNOLOGIES THAT AFFECT SAFETY OR EFFECTIVENESS, AND
    - IT POSES SAME TYPES OF QUESTIONS
    - HAS ACCEPTED SCIENTIFIC METHODS FOR EVALUATING
    - DATA DEMONSTRATE NO DIMINISHMENT OF PERFORMANCE

Attachment II

510(k) "SUBSTANTIAL EQUIVALENCE" DECISION-MAKING PROCESS (OVERVIEW)


New Device is Compared to Marketed Device*
Does New Device Have Same Intended Use?**
No
"Not Substantially Equivalent" Determination
Yes
Does New Device Have Technological Characteristics That Raise New Types of Safety or Effectiveness Questions?**
Yes
No
Require Information
Insufficient Information
Does Descriptive or Performance Information Demonstrate Equivalence?***
No
Yes
"Substantially Equivalent" Determination

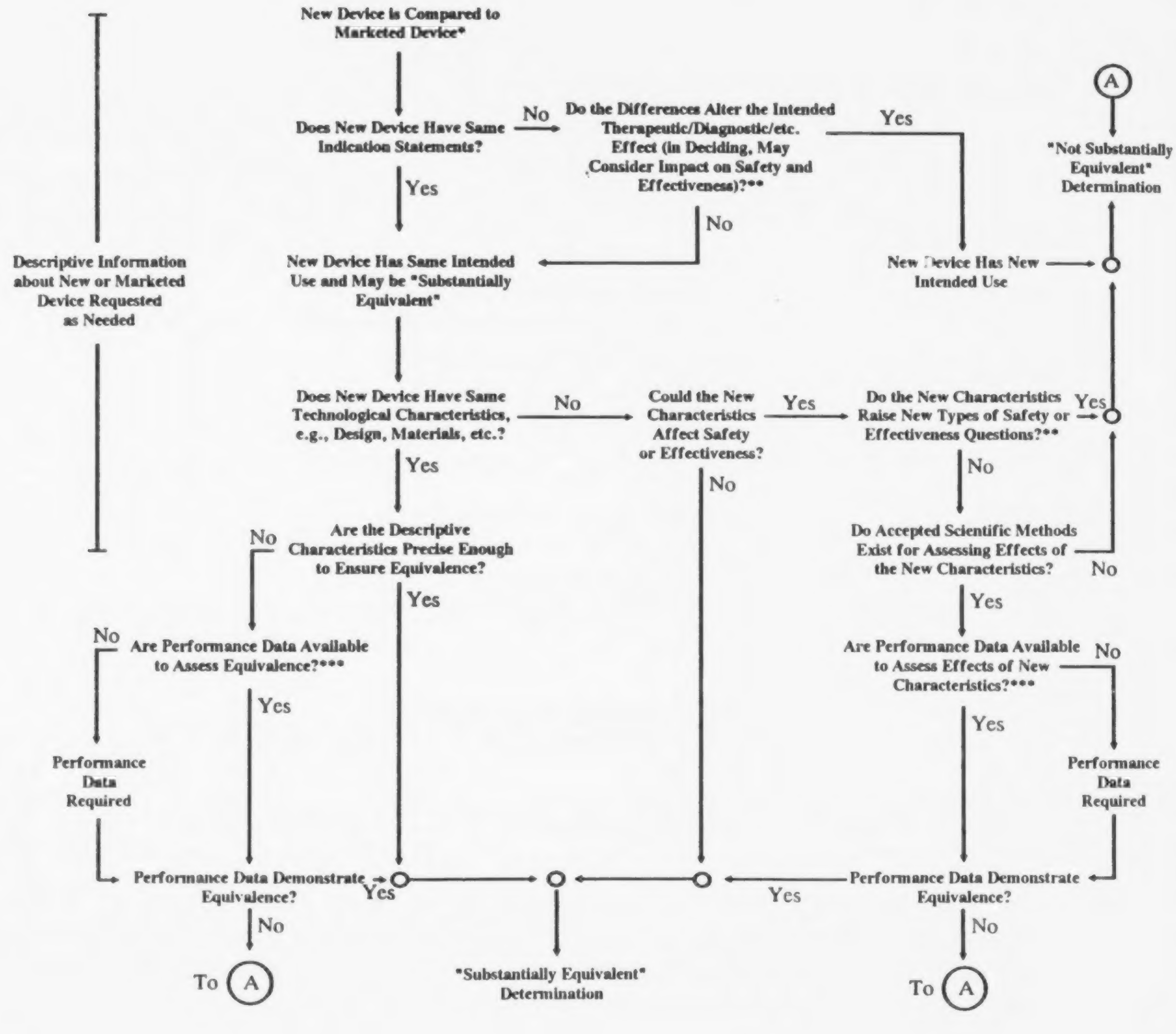
* 510(k) submissions compare new devices to marketed devices. FDA requests additional information if the relationship between marketed and "predicate" (pre-Amendments or reclassified post-Amendments) device is unclear.

** This decision is normally based on descriptive information alone, but limited testing information is sometimes required.

*** Data may be in the 510(k), other 510(k)s, the Center's classification files, or the literature.

Attachment III

510(k) "SUBSTANTIAL EQUIVALENCE" DECISION-MAKING PROCESS (DETAILED)


New Device is Compared to Marketed Device*
Does New Device Have Same Indication Statements?
No
Do the Differences Alter the Intended Therapeutic/Diagnostic/etc. Effect (in Deciding, May Consider Impact on Safety and Effectiveness)?**
Yes
A
"Not Substantially Equivalent" Determination
Yes
No
Descriptive Information about New or Marketed Device Requested as Needed
New Device Has Same Intended Use and May be "Substantially Equivalent"
New Device Has New Intended Use
Does New Device Have Same Technological Characteristics, e.g., Design, Materials, etc.?
No
Could the New Characteristics Affect Safety or Effectiveness?
Yes
Do the New Characteristics Raise New Types of Safety or Effectiveness Questions?**
Yes
Yes
No
No
No
Are the Descriptive Characteristics Precise Enough to Ensure Equivalence?
Do Accepted Scientific Methods Exist for Assessing Effects of the New Characteristics?
No
Yes
Yes
No
Are Performance Data Available to Assess Equivalence?***
Are Performance Data Available to Assess Effects of New Characteristics?***
No
Yes
Yes
Performance Data Required
Performance Data Required
Performance Data Demonstrate Equivalence?
Yes
Yes
Performance Data Demonstrate Equivalence?
No
No
To A
"Substantially Equivalent" Determination
To A

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* 510(k) submissions compare new devices to marketed devices. FDA requests additional information if the relationship between marketed and "predicate" (pre-Amendments or reclassified post-Amendments) devices is unclear.

** This decision is normally based on descriptive information alone, but limited testing information is sometimes required.

*** Data may be in the 510(k), other 510(k)s, the Center's classification files, or the literature.

MEDICAL DEVICE EXEMPTIONS

Below is a breakdown of both final and proposed 510(k) and GMP exemptions for Class I devices. To determine whether a device qualifies for exemptions, refer to the brief narrative "Identification" of the generic device in its final classification regulation. In many cases, the identification is specific as to the device's operating principle, design, composition, controls and intended use(s). A device's identification can be found by referring to the date and page number where its final regulation is printed in the **Federal Register ("FR Pg"** column below); the device's individual regulation number is cited in the **"21 CFR Part"** column. GMP exemptions apply only if the device is not labeled or otherwise represented as being sterile. Those 510(k) and GMP exemptions that have not been published in the **FR** as final are noted with a **"P"** for "proposed," final regulations are noted with an **"F"** for final.

FDA's decision to grant a 510(k) exemption is based on existing and reasonably foreseeable characteristics of commercially distributed devices within a generic type. Even if a device is granted this exemption, a 510(k) must be submitted for a new intended use or if the device is modified and uses a fundamentally new scientific technology than used in the device prior to May 28, 1976. At times, a 510(k) or GMP exemption is "with limitations" which is cited in the final rule describing the device. In such instances, the chart below carries a qualifying **"WL"** in the appropriate column. Often, "with limitations" applies only to devices "made of the same materials that were used in the device before May 28, 1976...." Another "with limitations" might be that the device does not touch the human body.

Reprints of the **FR** notices are available from **DSMA.** If unsure as to whether a given device falls under the generic identification to qualify for exemptions, a manufacturer should contact the CDRH contact person identified in the classification regulation.

	GMP	510 (k)	FR Pg	21 CFR Part
ANESTHESIOLOGY DEVICES				
Final GMP and 510(k) Exemption - 11/6/86 FR -- One anesthesiology device was classified with Ear, Nose and Throat Devices in this Federal Register.				
Tracheal tube cleaning brush	F	F	40388	868.5795
Final GMP Exemptions - 7/16/82 FR				
Ether hook	F		31147	868.5420
Nose clip	F		31150	868.6225
Manual algesimeter	F		31143	868.1030
Blow bottle	F		31147	868.5220
Rebreathing device	F		31148	868.5675
Cardiopulmonary emergency cart	F		31150	868.6175
Cuff spreader	F		31149	868.5760
Switching valve (ploss)	F		31145	868.1965
Posture chair for cardiac or pulmonary treatment	F		31147	868.5365

	GMP	510 (k)	FR Pg	21 CFR Part
Proposed 510(k) Exemptions - 1/20/88 FR				
Manual algesimeter		P	1581	868.1030
Esophageal stethoscope		P	1581	868.1910
Stethoscope head		P	1581	868.1930
Switching valve (ploss)		P	1581	868.1965
Blow bottle		P	1581	868.5220
Breathing tube support		P	1581	868.5280
Nasal oxygen cannula		P	1581	868.5340
Posture chair for cardiac or pulmonary treatment		P	1581	868.5365
Ether hook		P	1581	868.5420
Gas mask head strap		P	1581	868.5560
Breathing mouthpiece		P	1581	868.5620
Medicinal nonventilatory nebulizer (atomizer)		Pwl	1581	868.5640
Cuff spreader		P	1581	868.5760
Anesthetic cabinet, table or tray		P	1581	868.6100
Cardiopulmonary emergency cart		P	1581	868.6175
Nose clip		P	1581	868.6225
Anesthesia stool		P	1581	868.6700
Tracheobronchial suction catheter		Pwl	1581	868.6810

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CARDIOVASCULAR DEVICES

Proposed 510(k) Exemptions - 1/20/88 FR

Pacemaker service tools		P	1582	870.3730
Cardiopulmonary bypass accessory equipment		P	1582	870.4200
Cardiovascular surgical instruments		P	1582	870.4500

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CLINICAL CHEMISTRY AND CLINICAL TOXICOLOGY DEVICES

Final GMP and 510(k) Exemptions - 5/1/87 FR

General purpose lab equipment labeled or promoted for a specific medical use	F	F	16133	862.2050
[Only particular components of] Thin-layer chromotography system for clinical use	F		16134	862.2270

Final 510(k) Exemptions - 6/8/88 FR

Copper test system		F	21449	862.1190
Creatine test system		F	21449	862.1210
2,3-Diphosphoglyceric acid test system		F	21449	862.1255
Fatty acids test system		F	21449	862.1290

	GMP	510 (k)	FR Pg	21 CFR Part
Formiminioglutamic acid (FIGLU) test system		F	21449	862.1305
Gastric acidity test system		F	21449	862.1320
Glutathione test system		F	21449	862.1365
Hydroxybutyric dehydrogenase test system		F	21449	862.1380
Isocitric dehydrogenase test system		F	21449	862.1420
Lipid (total) test system		F	21449	862.1470
Lysozyme (muramidase) test system		F	21449	862.1490
Nitrogen (amino-nitrogen) test system		F	21449	862.1515
6-Phosphogluconate dehydrogenase test system		F	21449	862.1565
Phospholipid test system		F	21449	862.1575
Protein-bound iodine test system		F	21449	862.1640
Sorbitol dehydrogenase test system		F	21449	862.1670
Triose phosphate isomerase test system		F	21449	862.1720
Vitamin E test system		F	21449	862.1815
Calculator/data processing module for clinical use		F	21449	862.2100
Quinine test system		F	21450	862.3750
Sulphonamide test system		F	21450	862.3850

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DENTAL DEVICES

Final GMP and 510(k) Exemptions - 8/12/87 FR

Abrasive device and accessories	F		30104	872.6010
Articulator	F		30099	872.3150
Articulation paper	F		30105	872.6140
Base plate shellac	F		30105	872.6200
Dental X-ray film holder	F		30099	872.1905
Disposable flouride tray	F		30106	872.6870
Facebow	F		30100	872.3220
Impression tube	F		30105	872.6570
Intraoral dental wax	F		30106	872.6890
Manual toothbrush	F		30106	872.6855
Massaging pick or tip for oral hygiene	F		30105	872.6650
Pantograph	F	F	30102	872.3730
Performed impression tray	F		30106	872.6880
Prophylaxis cup	F		30105	872.6290
Resin applicator	F		30099	872.3140
Resin impression tray material	F		30102	872.3670
Rubber dam and accessories	F		30105	872.6300
Saliva absorber	F		30104	872.6050
Silicate protector	F		30105	872.6670

Proposed 510(k) Exemptions - 8/12/87 FR

Electrode gel for pulp tester		P	30121	872.1730
Mercury and alloy dispenser		P	30121	872.3080
Dental amalgam capsule		P	30122	872.3110

	GMP	510 (k)	FR Pg	21 CFR Part
Endodontic paper point		P	30122	872.3830
Massaging pick or tip for oral hygiene		P	30122	872.6650
Endodontic silver point		P	30122	872.3840
Gutta percha		P	30122	872.3850
Dental hand instrument		Pwl	30122	872.4565
Dental floss		Pwl	30122	872.6390
Resin applicator		P	30122	872.3140
Articulator		P	30122	872.3150
Facebow		P	30122	872.3220
Dental hand instrument		Pwl	30122	872.4565
Abrasive device accessories		P	30122	872.6010
Saliva absorber		P	30122	872.6050
Base plate shellac		P	30122	872.6200
Prophylaxis cup		P	30122	872.6290
Rubber dam and accessories		P	30122	872.6300
Impression tube		P	30122	872.6570
Massaging pick or tip for oral hygiene		P	30122	872.6650
Silicate protector		P	30123	872.6670
Manual toothbrush		P	30123	872.6855
Disposable flouride tray		P	30123	872.6870
Preformed impression tray		P	30123	872.6880
Dental X-ray film holder		P	30121	872.1905

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EAR, NOSE, AND THROAT DEVICES

Final GMP Exemptions - 11/6/86 FR

	GMP	510 (k)	FR Pg	21 CFR Part
Gustometer	F		40390	874.1500
Battery-powered artificial larynx	F		40391	874.3375
Prothesis modification instrument for ossicular replacement surgery	F		40391	874.3540
Ear, nose and throat drug administration device	F		40393	874.5220

Final GMP and 510(k) Exemptions - 8/25/87 FR

	GMP	510 (k)	FR Pg	21 CFR Part
Earphone Cushion for audiometric testing		Fwl	32111	874.1100
Prothesis modification instrument for ossicular replacement surgery	F	Fwl	32111	874.3540
Ear, nose, and throat manual surgical instrument		Fwl	32111	874.4420
External nasal splint		Fwl	32111	874.5800

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	GMP	510 (k)	FR Pg	21 CFR Part
GASTROENTEROLOGY-UROLOGY DEVICES				
Final GMP Exemptions - 11/23/83 FR				
Enema kit	F		53026	876.5210
Urine collector and accessories	F		53026	876.5250
Protective garmet for incontinence	F		53029	876.5920
Hernia support	F		53029	876.5970
Proposed 510(k) Exemptions - 1/20/88 FR				
Gastroenterology-urology evacuator		Pwl	1582	876.4370
Gastroenterology-urology fiberoptic retractor		P	1583	876.4530
Ribdam		P	1583	876.4560
Manual gastroenterology-urology surgical instrument and accessories		P	1583	876.4730
Urological table and accessories		Pwl	1583	876.4890
Continent ileostomy catheter		P	1583	876.5030
Hemodialysis system and accessories		Pwl	1583	876.5820
Ostomy pouch and accessories		P	1583	876.5900
Protective garment for incontinence		P	1583	876.5920

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	GMP	510 (k)	FR Pg	21 CFR Part
GENERAL AND PLASTIC SURGERY DEVICES				
Final GMP Exemptions - 6/24/88 FR				
Noninflatable extremity split	F		23874	878.3910
External aesthetic restoration prosthesis	Fwl		23874	878.3800
Proposed 510(k) Exemptions - 6/24/88 FR				
Noninflatable extremity split		Pwl	23882	878.3910
Speculum and accessories		Pwl	23881	878.1800
External facial fracture fixation appliance		Pwl	23882	878.3250
Plastic surgery kit and accessories		Pwl	23882	889.3925
Surgical camera and accessories		P	23882	878.4160
Manual surgical instrument for general use		Pwl	23882	878.4800
Manual operating table and accessories and manual operating chair and accessories		Pwl	23882	878.4950
Nonpneumatic tourniquet		Pwl	23882	878.5900

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GENERAL HOSPITAL AND PERSONAL USE DEVICES

Final GMP and 510(k) Exemptions - 10/21/80 FR

	GMP	510 (k)	FR Pg	21 CFR Part
Stand-on patient scale	F	F	69686	880.2700
Surgical sponge scale	F	F	69687	880.2740
Elastic bandage	F	F	69691	880.5075
Manual adjustable hospital bed	F		69693	880.5120
Nonpowered flotation therapy matress	F	F	69695	880.5150
Therapeutic medical binder	F	F	69696	880.5160
Neonatal eye pad	F		69699	880.5270
Medical absorbent fiber	F	F	69700	880.5300
Lamb feeding nipple	F	F	69708	880.5640
Pediatric position holder	F		69708	880.5680
Medical support stocking	F		69712	880.5780
Therapeutic scrotal support	F	F	69713	880.5820
Absorbent tipped applicator	F	F	69714	880.6025
Ice bag	F	F	69715	880.6050
Medical disposable bedding	F		69716	880.6060
Bed board	F	F	69716	880.6070
Cardiopulmonary resuscitation board	F	F	69717	880.6080
Hot/cold water bottle	F	F	69717	880.6085
Medical chair and table	F	F	69718	880.6140
Specimen container	F	F	69720	880.6175
Cast cover	F	F	69720	880.6185
Mattress cover for medical purposes	F		69721	880.6190
Ring cutter	F	F	69722	880.6200
Tongue depressor	F	F	69722	880.6230
Patient examination glove[1] /	F	F	69723	880.6250
Examination gown	F	F	69724	880.6265
Battery-powered medical examination light	F	F	69725	880.6350
Liquid medication dispenser	F	F	69727	880.6430
Skin pressure protectors	F	F	69727	880.6450
Body waste receptacle	F	F	69729	880.6730
Protective restraint	F	F	69730	880.6760
Manual patient transfer device	F	F	69731	880.6785
Washers for body waste receptacles	F	F	69731	880.6800
Medical disposable scissors		F	69732	880.6820
Hand carried stretcher	F		69735	880.6900
Irrigating syringe	F	F	69736	880.6960
Vein stabilizer	F	F	69737	880.6980

Proposed 510(k) Exemptions - 1/20/88 FR

	GMP	510 (k)	FR Pg	21 CFR Part
Hydraulic adjustable hospital bed		P	1583	880.5110
Manual adjustable hospital bed		P	1583	880.5120

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[1] / The January 13, 1989 FR revoked the 510(k) and GMP exemptions for patient exam gloves.

	GMP	510 (k)	FR Pg	21 CFR Part
Non-AC-powered patient lifts		P	1583	880.5510
Ultrasonic cleaner for medical instruments		Pwl	1583	880.6150
Medical insole		P	1583	880.6280
Liquid crystal vein locator		P	1584	880.6970

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HEMATOLOGY AND PATHOLOGY DEVICES

Final GMP Exemptions - 9/12/80 FR

	GMP	510 (k)	FR Pg	21 CFR Part
Dye and chemical solution stains	F		60583	864.1850
Tissue processing equipment	F		60587	864.3010
Microscopes and accessories	F		60590	864.3600
General purpose reagent	F		60592	864.4010
Cell and tissue culture supplies and equipment	F		60584	864.2240

Proposed 510(k) Exemptions - 1/20/88 FR

	GMP	510 (k)	FR Pg	21 CFR Part
Dye and chemical solution stains		P	1577	864.1850
Synthetic cell and tissue culture media and components		P	1577	864.2220
Cell and tissue culture supplies and equipment		P	1577	864.2240
Chromosome culture kit		P	1577	864.2260
Mycoplasma detection media and components		P	1577	864.2360
Animal and human sera		P	1577	864.2800
Balanced salt solutions or formulations		P	1577	864.2875
Tissue processing equipment		P	1578	864.3010
Specimen transport and storage container		Pwl	1578	864.3250
Cytocentrifuge		P	1578	864.3300
Device for sealing microsections		P	1578	864.3400
Microscopes and accessories		P	1578	864.3600
Automated slide stainer		P	1578	864.3800
Automated tissue processor		P	1578	864.3875
General purpose reagent		P	1578	864.4010
Enzyme preparations		P	1578	864.4400
Automated sedimentation rate device		P	1578	864.5800
Automated slide spinner		P	1578	864.5850
Capillary blood collection tube		Pwl	1578	864.6150
Manual blood cell counting device		P	1578	864.6160
Osmotic fragility test		P	1578	864.6600
Erythrocyte sedimentation rate test		P	1578	864.6700
Blood cell dilutent		P	1578	864.8200
Red cell lysing agent		P	1578	864.8540

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	GMP	510 (k)	FR Pg	21 CFR Part
IMMUNOLOGY AND MICROBIOLOGY DEVICES				
Final GMP and 510(k) Exemptions - 11/9/82 FR				
Wood's fluorescence lamp	F	F	50826	866.2600
Automated medium dispensing and stacking device	F	F	50826	866.2440
Anaerobic chamber	F	F	50825	866.2120
Microbiological incubator	F	F	50826	866.2540
Manual colony counter	F	F	50825	866.2180
Complement reagent		F	50834	866.4100
Radial immunodiffusion plate		F	50834	866.4800
Proposed 510(k) Exemptions - 1/20/88 FR				
Staphylococcal typing bacteriophage		P	1579	866.2050
Automated colony counter		P	1579	866.2170
Multipurpose culture medium		P	1579	866.2300
Differential culture medium		P	1579	866.2320
Enriched culture medium		P	1579	866.2330
Microbiological assay culture medium		P	1579	866.2350
Selective culture medium		P	1579	866.2360
Supplement for culture media		P	1579	866.2450
Quality control kit for culture media		P	1579	866.2480
Microtiter diluting and dispensing device		P	1579	866.2500
Microbial growth monitor		P	1579	866.2560
Gas-generating device		P	1579	866.2580
Microorganism differentiation and identification device		P	1579	866.2660
Acinetobacter calcoaceticus serological reagents		P	1579	866.3010
Adenovirus serological reagents		P	1579	866.3020
Arizona spp. serological reagents		P	1579	866.3035
Bordetella spp. serological reagents		P	1579	866.3065
Citrobacter spp. serological reagents		P	1579	866.3125
Echovirus serological reagents		P	1580	866.3205
Erysipelothrix rhusiopathiae serological reagents		P	1580	866.3250
Escherichia coli serological reagents		P	1580	866.3255
Flavobacterium spp. serological reagents		P	1580	866.3270
Influenza virus serological reagents		P	1580	866.3330
Klebsiella spp. serological reagents		P	1580	866.3340
Parainfluenza virus serological reagents		P	1580	866.3400
Proteus spp. (Weil-Felix) serological reagants		P	1580	866.3410
Reovirus serological reagents		P	1580	866.3470
Rhinovirus serological reagents		P	1580	866.3490
Rubeola (measles) virus serological reagents		P	1580	866.3520
Serratia spp. serological reagents		P	1580	866.3630
Staphylococcus aureus serolog. reagents		P	1580	866.3700

	GMP	510 (k)	FR Pg	21 CFR Part
Immunoelectrophoresis equipment		P	1580	866.4500
Immunofluorometer equipment		P	1580	866.4520
Immunonephelometer equipment		P	1580	866.4540
Ouchterlony ager plate		P	1580	866.4600
Rocket immunoelectrophoresis equipment		P	1580	866.4830
Support gel		P	1580	866.4900
Seminal fluid (sperm) immunological test system		P	1580	866.5800

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NEUROLOGICAL DEVICES

Final GMP Exemptions - 9/4/79 FR

Two-point discriminator	F		51731	882.1200
Esthesiometer	F		51737	882.1500
Tuning fork	F		51738	882.1525
Percussor	F		51741	882.1700

Proposed 510(k) Exemptions - 1/20/88 FR

Two-point discriminator		Pwl	1584	882.1200
Esthesiometer		Pwl	1584	882.1500
Tuning fork		P	1584	882.1525
Percussor		Pwl	1584	882.1700
Pinwheel		Pwl	1584	882.1750
Clip rack		Pwl	1584	882.4215
Neurosurgical suture needle		Pwl	1584	882.4650

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OBSTETRICAL AND GYNECOLOGICAL DEVICES

Proposed 510(k) Exemptions - 1/20/88 FR

Fetal stethescope		P	1585	884.2900
Obstetric and gynecologic general manual instrument		P	1585	884.4520
Vaginal insufflator		P	1585	884.5920

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OPHTHALMIC DEVICES

Final GMP Exemptions - 9/2/87 FR

Retinoscope	F		33359	886.1780
Ophthamic eye shield	F		33362	886.4750

Final GMP and 510(k) Exemptions - 9/14/88 FR

	GMP	510 (k)	FR Pg	21 CFR Part
Ocular esthesiometer	F	Fwl	35603	886.1040
Ophthalmic chair [manual]	F	F	35603	886.1140
Visual acuity chart	F	F	35603	886.1150
Color vision tester	F	F	35603	886.1170
Distometer	F	F	35603	886.1190
Optokinetic drum	F	F	35604	886.1200
Fornixscope	F	F	35604	886.1320
Amsler grid	F	F	35604	886.1330
Keratoscope	F	F	35604	886.1350
Bagolini lens	F	F	35604	886.1375
Diagnostic condensing lens	F	F	35604	886.1380
Flexible diagnostic Fresnel lens	F	F	35604	886.1390
Diagnostic Hruby fundus lens	F	F	35604	886.1395
Maddox lens	F	F	35604	886.1400
Ophthalmic trial lens clip	F	F	35604	886.1410
Ophthalmic trial lens frame	F	F	35604	886.1415
Stereopsis measuring equipment	F	F	35605	886.1460
Headband mirror	F	F	35605	886.1500
Perimeter	F	F	35605	886.1605
Ophthalmic bar prism	F	F	35605	886.1650
Ophthalmic Fresnel prism	F	F	35605	886.1655
Ophthalmic rotary prism	F	F	35605	886.1665
Pupillometer	F	F	35605	886.1700
Manual refractor	F	F	35605	886.1770
Nearpoint ruler	F	F	35605	886.1790
Tangent screen (campimeter)	F	F	35605	886.1810
Simulation (including crossed cylinder)	F	F	35605	886.1840
Ophthalmic instrument stand	F	F	35606	886.1860
Stereoscope	F	F	35606	886.1870
Fusion and stereoscopic target	F	F	35606	886.1880
Nystagmus tape	F	F	35606	886.1905
Spectacle dissociation test system	F	F	35606	886.1910
Ophthalmic knife test drum	F	F	35606	886.4230
Opthalmic operating spectacles (loupes)	F	F	35606	886.4770
Ophthalmic instrument table	F	F	35606	886.4855
Low-power binocular loupe	F	F	35607	886.5120
Low-vision magnifier	F	F	35607	886.5540
Ptosis crutch	F	F	35607	886.5600
Ophthalmic bar reader	F	F	35607	886.5800
Ophthalmic prism reader	F	F	35607	886.5810
Magnifying spectacles	F	Fwl	35607	886.5840
Low-vision telescope	F	F	35607	886.5870
Image intensification vision aid	F	F	35607	886.5910
Optical vision aid	F	F	35607	886.5915
Exophthalmometer		F	35604	886.1270
Ophthalmic lens gauge		F	35604	886.1420
Gonioscopic prism		Fwl	35605	886.1660
Schirmer strip		Fwl	35605	886.1800
Operating headlamp		F	35606	886.4335

	GMP	510 (k)	FR Pg	21 CFR Part
Manual ophthalmic surgical instrument		Fwl	35606	886.4350
Ocular surgery irrigation device		Fwl	35606	886.4360
Permanent magnet	F	F	35606	886.4445
Ophthalmic surgical marker	F	Fwl	35606	886.4570
Contact lens inserter/remover		F	35607	886.5420
Prescription spectacle lens		Fwl	35607	886.5844

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ORTHOPEDIC DEVICES

Final GMP and 501(k) Exemptions - 9/4/87 FR

Nonpowered dynamometer		F	33704	888.1250
Nonpowered goniometer		F	33704	888.1520
Calipers for clinical use		F	33710	888.4150
Depth gauge for clinical use		F	33710	888.4300
Orthopedic manual surgical instrument		Fwl	33711	888.4540
Protractor for clinical use		F	33711	888.4600
Template for clinical use		F	33711	888.4800
Nonpowered orthopedic traction apparatus and accessories	F	F	33711	888.5850
Noninvasive traction component	F		33711	888.5890
Cast component	F		33711	888.5940
Manual cast application and removal instrument	F		33711	888.5980

Proposed 510(k) Exemptions - 9/4/87 FR

Cement dispenser		Pwl	33715	888.4200
Cement mixer for clinical use		Pwl	33715	888.4210
Cement monomer vapor evacutor		P	33715	888.4220
Cement ventilation tube		Pwl	33716	888.4230
Noninvasive traction component		P	33716	888.5890
Cast component		Pwl	33716	888.5940
Manual cast application and removal instrument		P	33716	888.5980

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PHYSICAL MEDICINE DEVICES

Final GMP and 501(k) Exemptions - 11/23/83 FR

Plinth	F	F	53049	890.3520
Arm sling	F	F	53049	890.3640
Wheelchair accessory	F	F	53050	890.3910
Daily activity assist device	F	F	53050	890.5050
Exercise component	F	F	53052	890.5350

	GMP	510 (k)	FR Pg	21 CFR Part
Nonmeasuring exercise equipment	F	F	53052	890.5370
Prosthetic and orthotic accessory	F	F	53048	890.3025
Cane	F	F	53048	890.3075
Crutch	F	F	53048	890.3150
External limb orthotic component	F	F	53048	890.3410
External limb prosthetic component	F	F	53048	890.3420
Limb orthosis	F	F	53048	890.3475
Truncal orthosis	F	F	53049	890.3490
Congenital hip dislocation abduction splint	F	F	53049	890.3665
Denis Brown splint	F	F	53049	890.3675
Cane, crutch, and walker tips and pads	F	F	53050	890.3790
Mechanical walker	F	F	53050	890.3825
Cold pack	F	F	53052	890.5700
Moist heat pack	F	F	53053	890.5730
Traction accessory	F		53053	890.5925
Electrode cable	F		53047	890.1175
Nonpowered communication system	F		53049	890.3700
Wheelchair Platform scale	F		53050	890.3940
Nonpowered sitz bath	F		53051	890.5125

Proposed 510(k) Exemptions - 1/20/88 FR

Nonpowered communication system		P	1585	890.3700
Nonpowered sitz bath		P	1585	890.5125

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RADIOLOGY DEVICES

Final GMP and 510(k) Exemptions - 1/20/88 FR

Radiographic film		F	1570	892.1840
Radiographic head holder	F	F	1570	892.1920
Radiologic quality assurance instrument	F	F	1570	892.1940
Radiographic anthropomorphic phantom	F	F	1570	892.1950

Proposed 510(k) Exemptions - 1/20/88 FR

Nuclear anthropomorphic phantom		P	1589	892.1370
Nuclear flood source phantom		P	1589	892.1380
Nuclear sealed calibration source		P	1589	892.1400
Radionuclide test pattern phantom		P	1590	892.1420
Wall mounted radiographic cassette holder		P	1590	892.1880
Personnel protective shield		P	1590	892.6500

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APPENDIXES

A. SAMPLE PREMARKET NOTIFICATION LETTERS

Sample 1. for Class I Device
Sample 2. for Class II Device
Sample 3. for Modified Class II Device
Sample 4. for Class II Device With Clinical Data
Sample 5. for Class III Device

B. 510(k) RESPONSE LETTERS

- Substantially Equivalent Letter
- Not Substantially Equivalent Letter
- Cannot Determine Equivalency Letter - Need More Information

C. PREMARKET NOTIFICATIONS: THE FIRST 24,000 (MDDI JAN. 1986)

APPENDIX A: SAMPLE PREMARKET NOTIFICATION LETTERS

Sample 1 - For Class I Device

October 3, 1988

Food and Drug Administration
Center for Devices and Radiological Health
Document Mail Center (HFZ-401)
5600 Fishers Lane
Rockville, Maryland 20857

Re: 510(k) Submission Hydraulic
Adjustable Hospital Bed

Attention: Document Mail Clerk

XYZ Company, Inc., is requesting marketing clearance for its Hydraulic Adjustable Hospital Bed to be manufactured by ABC Device Company, Inc. The Premarket Notification information required by 21 CFR 807.87 is as follows:

a. Classification Name: Hydraulic Adjustable Hospital Bed
Common/Usual Name: Hospital Bed
Proprietary Name: XYZ Hospital Bed

b. Establishment Registration Number: A form FD 2891 was recently submitted for our distribution facility located at 100 Main Street, Anytown, NJ. We are awaiting receipt of our FDA registration number.

c. Classification: In the FEDERAL REGISTER notice of August 24, 1979, relative to medical devices reviewed by the General Hospital and Personal Use Device Classification Panel, FDA identified Hydraulic Adjustable Hospital Beds as a Class I device with no exemptions.

d. Performance Standards: Not applicable

e. Label/Labeling/Advertisements: Draft copies of the package labeling and promotional material for the XYZ Hospital Bed are enclosed (Exhibit #1).

f. Substantial Equivalence: The XYZ Hospital Bed will be contract manufactured for us by ABC Device Company, Inc., and is identical to that marketed by the American Medical Company since 1971. Copies of the specifications and mechanical drawings of our bed and for American Medical Company's preamendment product are enclosed (Exhibit #2). Copies of the package labeling and promotional literature for the ABC Hospital Bed are also enclosed (Exhibit #3).

We would appreciate your earliest attention to this 510(k) submission. The XYZ Hospital Bed will be displayed at a trade show later this month, but will not be offered for sale unless we first receive FDA clearance of our 510(k). Please do not hesitate to contact me at (215) 555-0100 if you have any questions regarding this submission.

Sincerely yours,

Enclosures

Sample 2 - For Class II Device
(With statement of confidentiality)

October 3, 1988

Food and Drug Administration
Center for Devices and Radiological Health
Document Mail Center (HFZ-401)
5600 Fishers Lane
Rockville, Maryland 20857

RE: 510(k) Notification

Attention: Document Mail Clerk

This is to notify you of the intention by the XYZ Company, Inc., to manufacture and market the following device:

Classification Name: Not Known

Common/Usual Name: Urological Catheter

Proprietary Name: XYZ Uro Cath

Establishment Registration Number: 9876543

Classification: Urological catheters would most likely have been reviewed by the FDA Gastroenterology/Urology Device Classification Panel. We are not aware that this device has been classified by FDA.

Performance Standard: None established under Section 514

Labeling/Promotional Material: Labeled specimen and draft copies of promotional literature are enclosed along with a sample of the urological catheter.

Substantial Equivalence: This product is similar in design, composition (polyvinyl chloride) and function to the Pharmaseal Urological Catheter and the BARD CS Urological Catheter, both of which were marketed prior to May 28, 1976. Copies of the specification and labeling for these two products are enclosed.

We consider our intent to market this device as confidential commercial information and request that it be considered as such by FDA. We have not disclosed the intent to market this device to anyone except employees of our firm and have taken precautions to protect this confidentiality.

Sincerely yours,

Enclosures

Sample 3 - For Modified Class II Device

October 3, 1988

Food and Drug Administration
Center for Devices and Radiological Health
Document Mail Center (HFZ-401)
5600 Fishers Lane
Rockville, Maryland 20857

Re: Premarket Notification

Dear Document Control Clerk:

Pursuant to the requirements of Section 510(k) of the Food, Drug, and Cosmetic Act, notification is made of the intention of the XYZ Company, Inc., to modify our disposable surgical mask to incorporate an improved filter media.

The essence of this modification is the substitution of a web of polypropylene fiber for the micro fiberglas web used in our current product. The reason for this change is that a small percentage of users of masks containing Fiberglas filter media report skin sensitivity. Micro Fiberglas still provides an excellent filter media, and we estimate that over 85 percent of surgical masks sold use this material. It is not our intention to discontinue our present mask, but to offer a new product as an alternative for those who do not wish to use a Fiberglas media.

The ABC Device Co., Inc., has marketed a disposable surgical mask containing polypropylene fiber since 1975. Our proposed product is substantially equivalent to the ABC surgical mask. Labeled samples of the ABC product and our current and modified disposable surgical masks are enclosed. Our modified product has been tested for bacteria filtration efficiency, breathability, and primary skin sensitivity and has been found to be well within existing norms for similar products.

The FDA General and Plastic Surgery Device Classification Panel recommended that surgical masks be placed in Class II and be assigned low priority for the development of a performance standard. FDA has yet to publish in the FEDERAL REGISTER for comment a proposed classification regulation for this device.

Should you require further information, please contact me at (215) 555-0100.

Sincerely yours,

Enclosures

Sample 4 - For Class II Device With Clinical Data

October 3. 1988

Food and Drug Administration
Center for Devices and Radiological Health
Document Mail Center (HFZ-401)
5600 Fishers Lane
Rockville. Maryland 20857

Re: 510(k) Notification

Attention: Document Control Clerk

This is to notify you of the intention of ABC Laser Company. Inc.. to manufacture and market the following device:

Classification Name: Laser. Neodymium:YAG

Common or Usual Name: Neodymium:YAG Laser

Proprietary Name: Laserpro

Establishment Registration Number: 9912345

Classification: We are not aware of the classification for this product.

Performance Standard: None Established under Section 514
Laser Standard Under Part 1040 Performance Standards for Light Emitting Products Sections 1040.10 and 1040.11

Labeling/Promotional Material: See Enclosed Table of Contents

Clinical Studies: See Enclosed Table of Contents

Substantial Equivalence: This product is similar in design. composition. and function to the Neodymium:YAG Laser manufactured by the XYZ Laser Company which was the subject of Premarket Notification #K859234. Copies of the labeling for this product are enclosed (see Table of Contents).

Sincerely Yours.

Enclosures

Sample 4 - (Cont'd)

TABLE OF CONTENTS

510(k) for LaserPro Neodymium:YAG Laser

Enclosure	Pages	Description
A	1-45	Labeling and Promotional Literature for the LaserPro Neodymium:YAG LAser.
B	46-98	Labeling and Promotional Literature for the ProYAG Laser manufactured by XYZ Company.
C	99-100	Comparison Table of Features of LaserPro and ProYAG lasers.
D	101-135	Articles from The New England Journal of Medicine and The Lancet Magazine concerning the use of Neodymium:YAG Lasers in surgery.
E	136-157	Analysis of the articles in the New England Journal of Medicine and Lancet describing the device characteristics of the laser(s) used in the articles, the patient population, and criteria and variables studied.
F	158-289	Protocol for clinical trial including patient selection criteria and a description of how and when study was monitored and by whom.
G	290-330	Clinical Data generated in support of the substantial equivalence of the subject device.
H	331-410	Analysis of clinical data showing substantial equivalence of the subject device based on the device characteristics, patient population, criteria and variables studied.

Sample 5 - For Class III Device
(With statement of confidentiality)

October 3, 1980

Dr. Paul Parkman, Director
Center for Biologics Evaluation and Research
8800 Rockville Pike
Bethesda, Maryland 20892

Re: Premarket Notification

Dear Sirs:

In accordance with Section 510(k) of the Federal Food, Drug, and Cosmetic Act, and in conformance with 21 CFR 807, this premarket notification is being submitted at least 90 days prior to the date when XYZ Device Company, Inc. proposes to introduce into interstate commerce for commercial distribution a Blood Cell Separator System to be known as the XYZ Model BCSI.

The following information is being submitted in conformance with 21 CFR 807.87:

1. Classification Name: Automated Blood Cell Separator*
   Common/Usual Name: Automated Blood Cell Separator
   Trade/Proprietary Name: XYZ Model BCSI

2. Establishment Registration Number:

   XYZ Device Company, Inc., will soon submit form FD 2891 (Initial Registration of Medical Device Establishment) for its manufacturing facility located at 100 Main Street, Anytown, CA.

3. FDA has classified Automated Blood Cell Separators in Class III. Final order was published in the FEDERAL REGISTER of September 12, 1980. The device was reviewed by the Hematology Device Classification Panel.

4. No performance standards applicable to Automated Blood Cell Separators have been established by the Food and Drug Administration.

5. Draft labeling and the Operator's Manual for XYZ Model BCSI are enclosed. Promotional literature and advertisements for the device have yet to be prepared.

6. The XYZ Model BCSI is substantially equivalent to the ABC Model B Continuous Flow Blood Cell Separator marketed since 1975 by ABC Labs, Inc. The equivalence of the ABC and XYZ blood cell separators is supported by the following attachments:

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*Note: The 510(k) for this device is reviewed by the Center for Biologics Evaluation and Research. Submissions should be addressed to that office as shown above.

Sample 5 - (Cont'd)

Enclosure I - Comparison of Features and Principles of Operation of ABC and XYZ Systems

Enclosure II - ABC Brochure (7/75)

Enclosure III - Draft III - Draft labeling and Operator's Manual - XYZ Model BCSI

Enclosure IV - Labeling and Operator's Manual - ABC Model B Continuous Flow Blood Cell Separator

Enclosure V - The XYZ Model BCSI Blood Cell Separator blood and fluid path materials are chemically and biologically comparable to those used with the ABC Model B Continuous Flow Blood Cell Separator. The types of tests and test results on which this determination is based are enclosed.

The XYZ Model BCSI Blood Cell Separator differs from the ABC Model B Continuous Flow Blood Cell Separator in the following respects:

1. Sterile, non-pyrogenic, and completely disposable, blood processing pathway through the use of polyvinyl chloride bag rather than a reusable polycarbonate bowl and seal.
2. Seal-less centrifugation reduces the possibility of blood leakage, or air or bacteria entry into the system.
3. Improved system monitoring affording greater donor safety through the use of microprocessor control in addition to operator monitoring.

XYZ Device Company, Inc., requests that the Food and Drug Administration hold as confidential information our intent to market the XYZ Model BCSI Blood Cell Separator.

We consider our intent to market this device to be confidential commercial information and, therefore, exempt from public disclosure. To the best of my knowledge, neither I nor anyone else has disclosed through advertising or any other manner, our intent to market the device to scientists, market analysts, exporters, or other individuals, except employees of, or paid consultants to, our company or individuals in an advertising or law firm pursuant to commercial arrangements with appropriate safeguards for safeguards for secrecy.

We have taken precautions to protect the confidentiality of the intent to market the device. We understand that the submission to the government of false information is prohibited by 18 U.S.C. 1001 and 21 U.S.C. 331(q). If you have any questions or require additional information or data, please call me at (213) 555-1234.

Sincerely yours,

Enclosures

(Only Enclosure I is in this Unit).

Sample 5 - (Cont'd)

Enclosure I

COMPARISON OF FEATURES AND PRINCIPLES OF OPERATION

Parameter	ABC Model B	XYZ Model BCSI
Mode of Operation	Continuous flow differential centrifugation	Continuous flow dual chamber differential centrifugation -Automatic or manual operation
Major Separate System Components	-Console control unit -Peristaltic pumps -Centrifuge rotor chamber -Sterile. disposable tubing kit -Sterilizable bowl assembly including upper stainless steel seal. lower ceramic seal. and silicone "O" rings	-Console control unit -Peristaltic pumps -Centrifuge rotor chamber (temp. controlled) -Sterile. disposable Apheresis pack and tubing kit
Console Specifics		
Size	30"w x 33"d x 41"h without optional side pumps	25"w x 36"d x 53"h
Weight	350 lbs.	600 lbs.
Electrical Requirements	115V. 15 amp. 50/60 Hz service. power outlet to be grounded and polarized	115V. 15 amp. 50/60 Hz service. power outlet to be grounded and polarized
Centrifuge Specifics		
Maximum RPM	3000	1400
Maximum Cent. Force	660 x g	285 x g
Typical Flow Rates	40-50 ml/min.	25-35 ml/min.
Pumps	Peristaltic (5) (2 additional peristaltic pumps available as an option)	Peristaltic (2)
Centrifugal Separation Chamber	Polycarbonate bowl	Polyvinyl chloride bag
Method of joining rotating (centrifuge) and non-rotating (donor) interface	2-piece seal. stainless steel and ceramic. lubricated with sterile saline solution	Seal-less. via rotating tube of Apheresis pack

Sample 5 (Cont'd)

Enclosure 1

Comparison of Features and Principles of Operation

Parameter	ABC Model B	XYZ Model BCSI
Fluid pathway	Sterile, non-pyrogenic, and disposable except for reusable bowls and seal which must be cleaned and sterilized prior to each procedure	Sterile, non-pyrogenic and disposable
System Printing Volume	270 ml sterile 0.9% sodium chloride solution with 1 USP unit Heparin/ml	300 ml sterile 0.9% sodium chloride solution
Maximum Extracorporeal Volume	270 ml	300 ml
Monitoring Systems		
Systems, General		
-Pump speed	Manual	Manual/Automatic
-Rotor speed	Manual	Manual/Automatic
-Rotor balance	Not applicable	Automatic
-Rotor chamber temp.	Not applicable	Automatic
-Fluid leak, rotor chamber	Visual	Automatic/Visual
-Door interlock	Not applicable	Automatic
-Microprocessor function	Not applicable	Automatic
-Procedure completion	Manual	Automatic
System, Fluid Path		
-Additive fluid levels	Anticoagulant only: automatic by weight sensing. Saline, prime, and lubricant: visual	Automatic/Visual
-Donor/inlet line occlusion	Automatic	Automatic
-Plasma/red cell interface	Visual	Automatic
-Donor/return line occlusion	Visual	Automatic
-Air in system	Automatic	Automatic

APPENDIX B: 510(k) RESPONSE LETTERS

SUBSTANTIALLY EQUIVALENT 510(k) LETTER: CLASSIFIED AND NOT CLASSIFIED

Re: [510(k) NUMBER]
Trade Name: ( )
Regulatory Class:
Dated:
Received:

Dear (ADDRESSEE):

We have reviewed your Section 510(k) notification of intent to market the device referenced above and we have determined the device is substantially equivalent to devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments. You may, therefore, market the device, subject to the general controls provisions of the Federal Food, Drug, and Cosmetic Act (Act). The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, and labeling; and prohibitions against misbranding and adulteration.

If your device is classified (see above) into either Class II (Performance Standards) or Class III (Premarket Approval), it may be subject to such additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 895. In addition, the Food and Drug Administration (FDA) may publish further announcements concerning your device in the Federal Register. Please note: this response to your premarket notification submission does not affect any obligation you might have under the Radiation Control for Health and Safety Act of 1968, or other Federal LAWS OR REGULATIONS.

This letter immediately will allow you to begin marketing your device as described. An FDA finding of substantial equivalence of your device to a preamendments device results in a classification for your device and permits your device to proceed to the market, but it does not mean that FDA approves your device. Therefore, you may not promote or in anyway represent your device or its labeling as being approved by FDA. If you desire specific advice on the labeling for your device, please contact the Division of Compliance Operations, Regulatory Guidance Branch (HFZ-323) at (301) 427-8040. Other general information on your responsibilities under the Act may be obtained from the Division of Small Manufacturers Assistance at their toll free number 800-638-2041 or at (301) 443-6597.

Sincerely yours,

NOT SUBSTANTIALLY EQUIVALENT 510(k) LETTER

Re: [510(k) NUMBER]
Trade Name: ( )
Regulatory Class: III
Dated:
Received:

Dear (ADDRESSEE):

We have reviewed your Section 510(k) notification of intent to market the device referenced above. We have determined the device is not substantially equivalent to devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to any device which has been reclassified into Class I (General Controls) or Class II (Performance Standards). This decision is based on the fact that ( ).

Therefore, this device is classified by statute into Class III (Premarket Approval), under Section 513(f) of the Federal Food, Drug, and Cosmetic Act (Act).

Section 515(a)(2) of the Act requires a Class III device to have an approved premarket approval application (PMA) before it can be legally marketed, unless the device is reclassified.

Any commercial distribution of this device prior to approval of a PMA, or the effective date of any order by the Food and Drug Administration re-classifying this device into Class I or II, would be a violation of the Act. Clinical investigations of this device must be conducted in accordance with the investigational device exemptions (IDE) regulations.

If you wish to pursue the marketing of this device and need information or assistance for preparing PMA, IDE, or reclassification submissions, please contact the Division of Small Manufacturers Assistance at their toll free number 800-638-2041 or at (301) 443-6597.

Sincerely yours,

CANNOT DETERMINE EQUIVALENCY 510(k) LETTER -- NEED MORE INFORMATION

Re: [510(k) NUMBER]
Trade Name: ( )
Dated:
Received:

Dear (ADDRESSEE):

We have reviewed your Section 510(k) notification of intent to market the device referenced above. We cannot determine if the device is substantially equivalent to a device marketed prior to May 28, 1976, the enactment date of the Medical Device Amendments, based solely on the information you provided. In order for us to complete the review of your submission, we require ( ). We believe that this information is necessary for us to determine whether or not this device is substantially equivalent to a preamendments device with regard to its safety and effectiveness.

You may not market this device until 90 days after you have provided adequate information described above and required by 21 CFR 807.87(f) and (h). If you market the device without conforming to these requirements, you will be in violation of the Federal Food, Drug, and Cosmetic Act (Act). You may, however, distribute this device for investigational purposes to obtain clinical data, if needed to establish substantial equivalence. Clinical investigations of this device must be conducted in accordance with the investigational device exemption (IDE) regulations.

If the requested information is not received within 30 days, we will consider your premarket notification to be withdrawn and your submission will be deleted from our system. If you submit the requested information after 30 days, it will be considered and processed as a new 510(k); therefore, all information previously submitted must be re-submitted so that your new 510(k) is complete.

If you have any questions concerning the contents of this letter, please contact (DIVISION REPRESENTATIVE) at (301) 427-( ). If you need information or assistance concerning the IDE regulations, please contact the Division of Small Manufacturers Assistance at their toll free number 800-638-2041 or at (301) 443-6597.

Sincerely yours,

best copy available

APPENDIX C

(MDDI JAN. 1986)

PREMARKET NOTIFICATIONS: THE FIRST 24,000

CARL F. BLOZAN
and STEVEN A. TUCKER

The Medical Device Amendments of 1976 established a requirement that new marketers of medical devices—manufacturers, repackagers, and importers—submit premarket notifications (510[k]s) to FDA at least 90 days prior to marketing their products. (The premarket notifications are known as 510[k]s because the requirement for them is found in section 510[k] of the Federal Food, Drug, and Cosmetic Act.) The notifications submitted fall into two basic categories: (1) those submitted by firms seeking to enter markets in which they have not previously participated, with medical devices that are similar to those already being marketed by others (approvals in these cases lead to a greater availability of medical devices on the market), and (2) those submitted by firms seeking to market variations—presumably, improvements or other modifications—of products that they already market.

FDA does not actually "approve" a 510(k) submission but rather determines whether the proposed device is substantially equivalent to a type of device that was on the market before May 28, 1976. If this is found to be the case, the new device is allowed to enter interstate commerce. If a marketer presents insufficient evidence to support a judgment of equivalence, FDA may request additional evidence or may require the marketer to submit a premarket approval application (PMA) to show that the device is safe and effective before allowing it on the market.

Through the 510(k) process, FDA has focused on the performance of the device rather than on its physical configuration. Devices that achieve the same function but that are demonstrably safer or more effective because of technological innovation are thus routinely allowed on the market via a 510(k). The 510(k) process is designed to accommodate technological innovation within existing uses for medical devices. Therefore, the finding of substantial equivalence to a type of device on the market as of the 1976 date does not indicate a stagnation of technology.

Since 1976, FDA has received more than 25,000 510(k)s, compared with fewer than 400 PMAs for the same period. Clearly, the 510(k) process is the method of choice for marketing a new product. Compared to a

Year	Total Receipts of 510(k)s	Average Monthly Receipts of 510(k)s	Index of Monthly Receipts of 510(k)s (1976 = 100)
1976	1,362[a]	195	100
1977	2,427	202	104
1978	2,180	182	93
1979	2,724	227	116
1980	3,316	276	142
1981	3,649	304	156
1982	3,939	328	168
1983	4,616	385	197
Total	24,213	–	–

[a] This figure reflects 510(k) submissions for seven months of 1976.

Source: This table was developed by the authors from information made available by CDRH.

Table I: Number of 510(k) submissions received by FDA, 1976–1983.

Medical Specialty (Panel)[a]	Number of 510(k)s	Percentage of All 510(k)s	Percentage of All PMAs
Anesthesiology	1,616	6.7	4.2
Cardiovascular	3,001	12.4	9.5
Clinical chemistry/Toxicology	3,865	16.0	1.7
Dental	1,266	5.2	2.0
Ear, nose, and throat	888	3.7	1.1
Gastroenterology and urology	1,516	6.3	6.4
General and plastic surgery	1,936	8.0	4.5
General hospital	2,165	8.9	1.7
Hematology/Pathology	1,095	4.5	0.3
Immunology/Microbiology	2,394	9.9	11.7
Neurology	604	2.5	1.7
Obstetrics and gynecology	581	2.4	2.2
Ophthalmics	649	2.7	46.1
Orthopedics	805	3.3	3.9
Physical medicine	988	4.1	0.8
Radiology	779	3.2	2.2
Unknown	65	0.3	–
Total	24,213	–	–

[a] *Medical specialty* is synonymous with *panel*. *Panel* refers to one of 16 FDA advisory panels that grouped and classified all medical devices on the market in 1976.

Source: See Table I.

Table II: Percentage of 510(k) submissions by medical specialty, 1976–1983.

PMA, a 510(k) is not only easier and less expensive to prepare but is also processed faster by FDA and requires significantly fewer resources for agency review.

This article is intended to complement an earlier report that examined PMAs,[1] giving a total current picture of the FDA approval processes for medical devices. The first section describes trends in the number and purposes of 510(k)s, in the numbers of marketers, and in the findings of "substantial equivalence." The second section characterizes 510(k) submissions by size and content. The third section looks at the FDA review process, and the fourth section contains conclusions.

Some Trends in the 510(k) Process

Number and Purposes of 510(k)s. FDA's receipts of 510(k)s increased steadily from 1976 to 1983 (Table I). The monthly submission rate has almost doubled since the Medical Device Amendments were enacted, and the pace shows no sign of abating: the annual rate of increase since 1980 has been 15%, compared to 5% in earlier years. In 1984, 5058 510(k)s were submitted, for an average of 422 per month.

The increase in 510(k) submissions has been fairly uniform by medical specialty (panel) (see Table II). The proportions of 510(k)s by panel remained constant over the eight-year period in question, with no specialty exhibiting a consistent pattern of growth or decline.

More than 30% of all 510(k) submissions have been for clinical laboratory devices (clinical chemistry/toxicology, hematology/pathology, and immunology/microbiology). Cardiovascular devices are the next largest area of 510(k) activity. Every panel has at least 2.4% of the total.

The greatest difference between the proportion of 510(k)s and PMAs is shown for ophthalmic devices, largely because of the requirement that there be PMAs for all contact lenses and solutions. Cardiovascular and immunology/microbiology products have relatively high proportions of both 510(k)s and PMAs. Conversely, clinical chemistry/toxicology, general hospital, hematology/pathology, and physical medicine products account for much higher proportions of 510(k)s than of PMAs.

All medical devices and in vitro diagnostic products have been classified into device types. (The term *device type* as used in this article refers to FDA's publication in the *Federal Register* of a specific definition of the function(s) performed by a device; i.e., device type = regulation name). About 1800 device types have been either proposed or classified as final in the 16 medical specialties or panels. The scope of device type ranges from the very general (e.g., manual surgical instruments—forceps, clamps, scalpels, trocars, etc.) to the very specific (e.g., patellofemoral polymer/metal semiconstrained prosthesis, which is one of 12 artificial-knee device types).

The number of 510(k) submissions per device type during the 1976–1983 period ranged from 421 for manual surgical instruments to none for 461 device types. Marketers submitted 100 or more 510(k)s for each of 26 device types, and overall, one or more 510(k) submissions were made for three-quarters of all device types (Table III). While it is not possible to give reasons for any instance, 329—or 71%—of the 461 device types with no 510(k)s had two, one, or no manufacturers listed with FDA. Thus, these products most likely included those with limited market potential, those whose use may have been superseded by another device type, or those with some kind of marketing protection (e.g., a patent or licensing agreement).

Medical Specialty	Percentage of Device Types
Anesthesiology	81
Cardiovascular	87
Clinical chemistry/ Toxicology	77
Dental	76
Ear, nose, and throat	74
Gastroenterology and urology	76
General and plastic surgery	87
General hospital[a]	91
Hematology/Pathology	81
Immunology/Microbiology[a]	72
Neurology	52
Obstetrics and gynecology	67
Ophthalmics	64
Orthopedics	72
Physical medicine[a]	83
Radiology	75
Total	76

[a] These panels have exempted 55 device types from 510(k) requirements; the exempted devices were not included in the calculations.

Source: See Table I.

Table III: Percentage of device types in each medical specialty that have been the subject of 510(k) submissions, 1976–1983.

By class of device type, the averages for 510(k) submissions were as follows:

- Class I: 74% (devices such as canes, crutches, many diagnostic reagents, and most manual instruments, which are only required to meet general controls, including adherence to GMPs).
- Class II: 78% (devices such as powered instruments, most catheters, and monitoring equipment, which are subject to general controls and performance standards).
- Class III: 59% (devices that are subject to general controls and that will eventually require submission of safety and efficacy data in a PMA to FDA; examples are devices that are implanted in the body).

The observed 74% value for Class I devices may be low. Marketers of certain Class I device types are exempt from 510(k) requirements, but as of this writing nly three panels have completed the compilation of neir lists of exempt devices. Therefore, this figure robably understates the percentage of Class I device ypes requiring 510(k)s that have been the subject of 10(k) submissions. Given this, it could appear that the igher the class of a device type, the less likely it is to ave had a 510(k) submitted.

New and Existing Marketers of Device Types. The urpose of 510(k)s appears to be about evenly divided etween notifying FDA that the marketer is going to narket a device type that it had not marketed before nd notifying the agency about a modification, technical innovation, or addition of a new product within a device type that the marketer already markets.

A 510(k) from a marketer who had not listed[2] the device type with FDA by early 1980 (defined in this paper as a new marketer) was assumed to be notification of that marketer's initial entry into the market for that device type. Any subsequent 510(k)s from that marketer for the same device type, as well as 510(k)s from marketers who had listed their device type with FDA, were assumed to be for modifications, improvements, or expansions of product lines within the device type. These assumptions were necessary because it was not possible to determine the marketing intent for all 510(k)s. Marketers could have been marketing the device for a long time but not have listed it, so we are likely overcounting new market entry by the first assumption. On the other hand, there may well be significant expansions of product lines within one device type (e.g., adding forceps, scalpels, and trocars to already marketed clamps, all contained within the generic device type, manual surgical instruments) that represent new *products* to the marketer but that are not picked up by our definition of *device type*.

The percentage of 510(k)s that are assumed to represent initial market entry (i.e., the marketer had neither listed the device type nor submitted a previous 510(k) for the device type) increases as the number of 510(k)s received for the device type decreases. Generally, about 30% of the 510(k)s for device types in highly competitive markets (i.e., 40 or more listed marketers) represent the initial submission from new marketers, whereas about 60% of the 510(k)s for devices in very

Device Types with:	Number of 510(k)s	Percentage of 510(k)s from New Marketers	Overall Percentage of 510(k)s from New Marketers
40 or More Listed Marketers			
Manual surgical instruments	421	35	32
Selective culture media	315	9	
Hearing aids	286	16	
Quality control material	184	28	
Intravascular administration sets	169	36	
Differential culture media	134	14	
Electrical cutting and coagulating devices	129	33	
Gauzes and sponges	119	41	
Urine collectors	114	34	
Glucose test systems	111	28	
59 other device types	3,076	36	
3 to 39 Listed Marketers			
915 device types	17,223	49	46
2 or Fewer Listed Marketers			
49 with 10 or more 510(k)s	704	51	63
12 with 9 510(k)s	108	53	
15 with 8 510(k)s	120	63	
18 with 7 510(k)s	126	54	
27 with 6 510(k)s	162	69	
29 with 5 510(k)s	145	66	
38 with 4 510(k)s	152	70	
47 with 3 510(k)s	141	76	
74 with 2 510(k)s	148	80	
126 with 1 510(k)	126	94	
Total	24,213	—	44

Table IV: Number of 510(k)s and percentage of 510(k)s from new marketers for selected device types. 1976–1983.

Device Type	Number of 510(k)s	Number of Marketers Listing the Device Type as of Early 1980[a]	Number of Listed Marketers Who:		Number of New Marketers since January 1980
			Also Submitted 510(k)s	Did Not Submit 510(k)s	
Manual surgical instruments	421	279	50	229	103
Selective culture media	315	55	9	46	22
Hearing aids	286	42	16	26	35
Implantable pacemaker pulse generators	269	22	14	8	4
Pacemaker electrodes	220	20	12	8	8
Quality control material	184	57	30	27	28
Intravascular administration sets	169	54	15	39	44
Infusion pumps	146	26	12	14	34
Differential culture media	134	46	13	33	15
Electrical cutting and coagulating devices	129	53	12	41	23

[a] It is likely that some of these marketers (perhaps 20–25%, based on data from an unpublished longitudinal study of medical device establishments) have gone out of the medical device business since 1980. Similarly, some of the new marketers may no longer be active.

Table V: Number of new marketers and number of marketers listing the 10 device types with the most 510(k) and subsequent 510(k) activity.

limited markets (2 or fewer listed marketers) represent the first 510(k) from new marketers (Table IV). Although there were many listed marketers, some device types—e.g., selective culture media, differential culture media, and hearing aids—showed relatively low percentages of 510(k)s from new marketers. Only 9% of the 315 510(k)s for selective culture media represented the initial submission from marketers who had neither listed this device type nor submitted a previous 510(k). For the device types with 2 or fewer listers, the percentage of 510(k)s from a new marketer reached high levels (over 70%), indicating that listed marketers of these device types were not submitting many 510(k)s.

The overall average of 44% of 510(k)s as the initial submission from new marketers probably understates the number of 510(k)s representing new *products* for the marketer. This is so primarily because of the large amount of 510(k) activity in generic device types, as well as because changes in existing products marketed via a 510(k) may well reflect substantial improvement or innovation. The device would therefore be considered to be a new product by the marketer.

Table V provides some insights into the numbers of new marketers relative to the number of existing marketers, as well as into 510(k) activity for the 10 device types with the most 510(k) submissions. Items of interest from Table V include the following:

- For seven of the device types, far more than half of the listed marketers in 1980 did not submit even one 510(k) for the device type.
- With three exceptions (implantable pacemaker pulse generators, pacemaker electrodes, and quality control material), the number of new marketers exceeded the number of existing (listed) marketers who submitted 510(k)s for the device type.
- For one device type (infusion pumps), the number of new marketers exceeded the number of listed marketers in 1980.
- The number of new marketers of implantable pacemaker pulse generators and pacemaker electrodes was very small relative to the number of 510(k)s submitted.

Table VI is a comparison of the number of marketers who were listed with FDA for a particular device type in 1980 and the number of previously unlisted firms that first submitted 510(k)s for the device after 1980. The table reveals that new marketers tend to enter markets in which there are already many competing products rather than markets in which few devices are present. The association between new and listed marketers is shown to be very high.

The data in Table VII show that about 21% of all 510(k) submissions are for the 69 device types with 40

Medical Specialty (Panel)	Rank of Number of Marketers per Device Type before 1980	Rank of Number of New Marketers per Device Type Based on 510(k) Submissions after January 1980[a]
General and plastic surgery	1	1
General hospital	2	2
Physical medicine	3	5
Dental	4	13
Clinical chemistry/Toxicology	5	3
Gastroenterology and urology	6	11
Anesthesiology	7	8
Cardiovascular	8	4
Immunology/Microbiology	9	10
Ear, nose, and throat	10	15
Hematology/Pathology	11	7
Obstetrics and gynecology	12	9
Radiology	13	12
Orthopedics	14	6
Ophthalmics	15	14
Neurology	16	16

[a] The number of 510(k) submitters unlisted prior to 1980 is only a surrogate measure for new market entries, because some marketers who were not listed with FDA prior to 1980 may nonetheless have had devices on the market. To test the sensitivity of the association between the two rankings, the rankings were arbitrarily changed by two ranks for all medical specialties; the association remained statistically significant at the 90% level.

Source: See Table I.

Table VI: The rankings of the number of marketers per device type who listed in 1980, with the rankings of the number of new marketers per device type after 1980.

Number of Marketers Listed with FDA in 1980 per Device Type	Number of Device Types	Number of Listed Products	Percent of Listed Products	Number of 510(k)s	Percent of 510(k)s
2 or fewer	765	657	4	1,932	8
3 to 39	1,047	10,967	69	17,223	71
40 or more	69	4,267	27	5,058	21
Total	1,881[a]	15,891	100	24,213	100

[a] There were 1881 device types when the authors' data base was created in January 1980. These have been consolidated into 1720 device types, although the classification process is not yet complete.

Source: See Table I.

Table VII: Comparison of the number of listed products and the number of 510(k) submissions by the number of listing marketers per device type.

or more marketers in 1980. However, proportionately, the percentage of 510(k)s for device types that had 2 or fewer listed marketers in 1980 is double that of listed products for those 765 device types. Only 4% of all listed products (i.e., the sum of all of the marketers who listed each device type) were for device types with 2 or fewer listed marketers, yet 8% of all 510(k)s were for such device types.

While we know very little that is specific about the size of the markets, size of the marketers, etc., it is clear that 510(k) submissions reflect a sizable level of activity within most device types. There are a substantial number of new market entries, but there are an equal number of 510(k)s submitted for modifications, technological innovation, or expansions of product lines for device types already marketed by the submitters. Device types with many existing marketers appear to attract a disproportionate number of 510(k)s, yet the 510(k) process has proved to be an effective means of increasing the number of products on the market—especially those that had very few listed marketers in 1980.

As of the end of 1983, 4008 different marketers had submitted at least one 510(k) notification. Almost half the marketers had submitted only one, but 4 marketers accounted for 960 submissions—4% of all 510(k)s (Table VIII). Thirty firms had submitted 100 or more 510(k)s, and together they accounted for more than 4000 submissions. Sixty-eight percent of the 510(k)s came from the 522 marketers who submitted 10 or more 510(k)s each.

In addition, 178 individual researchers made a total of 230 submissions; 90% of the researchers submitted only one 510(k), but one person submitted 19. (Individual researchers are usually practicing physicians, dentists, or ophthalmologists who wish to market their own products.)

"Substantial Equivalence." Eighty-six percent of all 510(k)s submitted from 1976 to 1982 were for devices that were substantially equivalent to devices marketed before the enactment of the Medical Device Amendments (Table IX). Only 2% of the 510(k)s were declared nonequivalent. However, another 12% were not logged out (i.e., a final determination of equivalency or nonequivalency was not made). Reasons for a 510(k)'s not being logged out include the following:

- The prospective marketer has not responded to a request for additional information.
- The marketer has withdrawn the 510(k) notification.
- The FDA review is still in progress.
- The device is exempt from the 510(k) process.
- The product is not a medical device.
- The device is regulated as a drug.

Number of 510(k)s per Marketer	Number of Marketers	Cumulative Number of Marketers
1	1975	1975
2	592	2567
3	256	2823
4	215	3038
5	137	3175
6	97	3272
7	82	3354
8	69	3423
9	63	3486
10–14	183	3669
15–19	90	3759
20–29	105	3864
30–39	38	3902
40–49	34	3936
50–99	42	3978
100–199	26	4004
200+	4	4008

[a] The nature of the data base precludes definitive findings—for example, firm names are often entered with different formats (the use of "Co." results in a new entry), and some firms change names or ownership. The data base was edited to take account of some of these instances, but the authors cannot assure precision.

Source: See Table I.

Table VIII: Distribution of marketers by number of 510(k) submissions, 1976–1983.[a]

Summary. The significant findings presented thus far can be summarized as follows:

- The monthly rate of 510(k) submissions doubled in the first eight years following enactment of the requirement for premarket notification, and the rate continues to rise.
- The increase has occurred proportionately for all medical specialties.
- More than three-quarters of all device types have had some 510(k) activity.
- About half of all 510(k)s are the initial submission from new marketers of a device type. The other half are for modifications, improvements, or expansions of existing product lines.
- Most new marketers enter competitive markets, yet there has been substantial entry into noncompetitive markets.
- More than 4000 marketers have submitted at least 1 510(k). Half this number have submitted only 1; 30 marketers have each submitted 100 or more.
- About 86% of all 510(k) submissions are for devices found to be substantially equivalent to a device on the market when the 1976 Medical Device Amendments took effect.

Size and Content Characteristics of 510(k) Submissions

Although the average length of a sample of 162 logged-out 510(k) submissions[3] was 24 pages, half of the submissions had fewer than 10 pages. Only 4% of the 510(k)s in the sample exceeded 100 pages, with the longest submission being 207 pages. By comparison, PMAs average over 1000 pages.[4] The difference in size is attributable to the PMA reports on clinical trials. The case-report forms (i.e., the reports of individual patient data) alone account for at least half of the pages in a typical PMA, and the descriptions of the trials, protocols, and analyses of results account for many more pages. A PMA also contains a much more detailed description of the device and of how the device is to be manufactured.

What does the typical 510(k) submission contain? According to the regulations, each 510(k) should contain the following information:

- The device name (proprietary and common).
- The establishment registration number.
- The class of the device.
- Efforts to comply with any applicable performance standards.
- Proposed labels sufficient to describe the device.
- A statement indicating the similarities to and differences between the device and marketed products.
- Supporting statements for any significant changes in safety or effectiveness.

Because a great deal of this information is usually contained in the cover letter that accompanies the 510(k), much of a typical 510(k) submission consists of the catalogs and advertisements that show equivalence to competitors' products, the operating manuals and labeling that will accompany the new product, and so on. While most of a small sample of marketers acknowledged that 510(k) submissions require only information that is normally collected in the course of developing a product, they did report having had some difficulty in knowing how to submit these data.

We examined the 162 sample 510(k)s in detail and categorized their contents (Table X). Forty-eight percent of the sample included catalogs, averaging 13

Year	Number of 510(k)s	Number Logged Out	Percent Logged Out	Number Found Substantially Equivalent	Percent of Logged Out Found to Be Substantially Equivalent	Percent Submitted Found to Be Substantially Equivalent
1976	1,362	1,120	82	1,112	99	82
1977	2,427	2,190	90	2,144	98	88
1978	2,180	2,033	93	1,990	98	91
1979	2,724	2,491	91	2,447	98	90
1980	3,316	2,933	88	2,860	98	86
1981	3,649	3,360	92	3,297	98	90
1982	3,939	3,094	79	3,038	98	77
Total	19,597	17,221	88	16,888	98	86

Source: See Table I.

Table IX: Annual submissions of 510(k)s and outcomes as of March 20, 1984.

Type of Information	Total No. of Pages in 510(k) Sample	Percentage of Total Pages Represented by This Information	Number of 510(k)s Containing This Information	Percentage of 510(k)s Containing This Information	Average Number of Pages of This Information, if Present
Catalogs/Comparisons	1038	27	78	48	13.3
Advertisements	567	15	42	26	13.5
Operating manuals/ Instructions for use	540	14	20	12	27.0
Labels/Packages	435	11	106	65	4.1
Cover letters	372	10	162	100	2.3
Descriptions/ Quality assurance	243	6	11	7	22.1
Specifications/Drawings	218	6	19	12	11.5
Test results	192	5	8	5	24.0
Journal articles	126	3	13	8	9.7
Photographs/Samples	61	2	47	29	1.3
Protocols	27	1	3	2	9.0
Total	3819	100	—	—	—

Source: Developed by authors from the sample of 162 submissions.

Table X: Types of information contained in sample of 162 510(k) submissions.

pages in length. Operating manuals or instructions for use, present in roughly one of every eight 510(k)s, contributed an average of 27 pages to those submissions. (All 7 submissions with more than 100 pages included operating manuals.) Cover letters tended to be short (a little over 2 pages in length), and labeling, which was present in two-thirds of the submissions, averaged 4 pages in length. Three of the submissions included protocols for future studies, all of which were for product reliability (stability or sterility studies) rather than for safety and effectiveness trials.

As noted earlier, most 510(k) submissions are not costly to prepare. Based on a small sample, marketers' estimates of 510(k) preparation costs ranged from "about $50" to "a couple of thousand dollars." Six marketers said that their costs ranged from $200 to $500, but they cautioned that costs vary widely with the device. Most of the costs are attributable to time spent in legal review or time spent by the 510(k) preparer with the product development staff.

Summary. The average 510(k) consists of about 24 pages, although the median length is 10 pages. More than half of the average number of pages consist of comparisons to devices already on the market, usually shown through copies of catalogs, advertisements, and operating manuals and labels. The typical 510(k) submission is only one-fortieth the size of a PMA submission, with the main reason for the difference being the latter's inclusion of a detailed device description and analyses of clinical trials. Many types of information (e.g., operating manuals, device specifications, and journal articles) are present in fewer than one 510(k) out of every eight. The preparation of a 510(k) submission is not considered to be costly (generally under $500), and 510(k)s frequently make use of already collected information.

The FDA Review Process

As mentioned earlier, the manufacturer is required to submit a 510(k) 90 days prior to marketing a device. FDA has chosen to respond to 510(k)s within the 90-day period. While FDA is doing this for the majority of the submissions, some submissions do require substantially longer review times. When a 510(k) is received, FDA assigns it a control number, distributes the document to the review staff, notifies the marketer that the 510(k) was received, and starts the clock for the 90-day review period. A scientific reviewer examines the evidence that is submitted to determine whether the proposed device is substantially equivalent to a marketed product. If the information provided is adequate for a determination to be made, the reviewer makes a decision. Following a legal and administrative review of the decision, FDA notifies the marketer of the decision by letter.

A reviewer who requires information beyond that included in the original submission may obtain it informally, by telephone, or formally, by requesting an amendment to the 510(k). A formal amendment is considered a new submission and restarts the 90-day review period. As of mid-1984, a total of 5904 amendments had been submitted for the 24,213 original 510(k) submissions.

Table XI presents an analysis of review times and processes carried out using the same sample of 162 logged-out 1982 and 1983 510(k) submissions described earlier. One hundred forty-nine of those 510(k)s were found to be substantially equivalent, eight were found to be not substantially equivalent, and five were incorporated as amendments to previously submitted 510(k)s.

Review time for the sample of 510(k)s averaged 68 days. Review of the 5 510(k)s that were incorporated as amendments took only 30 days (which reflects only the time spent in deciding to treat them as amendments), whereas review of submissions found to be not equivalent averaged 124 days. Review of the 149 substantially equivalent 510(k)s averaged 67 days. By comparison, approval of the typical PMA takes 380 days.[5]

Review times for the sampled 1983 510(k) submissions were longer than were those for 1982. The average length of time for review of a 510(k) submitted in 1982 and found to be substantially equivalent was 57 days, compared with an average of 75 days for a 510(k) submitted in 1983. (Review resources were nearly constant during these years but have been increased recently.) These differences are not statistically significant at the 95% level. However, 28% of the sampled 510(k) submissions in 1983 took 90 days or longer to review, compared with 13% of the 1982 submissions. Such a difference is statistically different at the 95% confidence level.

Year	Total No. of 510(k)s in Sample	Substantially Equivalent			Not Substantially Equivalent			Incorporated as Amendments		
		Review Days*			Review Days			Review Days		
		No.	Mean	Median	No.	Mean	Median	No.	Mean	Median
1982	75	69	57	43	4	104	67	2	27	27
1983	87	80	75	57	4	144	105	3	32	37
Total	162	149	67	–	8	124	–	5	30	–

Table XI: FDA review time for a sample of 510(k) submissions.

Category	Number of Responses to Requests	Number Resolved by Phone	Average Number of Additional Pages Submitted
Catalogs/Comparisons	15	3	12.4
Advertisements	0	—	—
Operating manuals/Instructions for use	19	9	15.7
Labels/Packages	13	3	17.6
Cover letters	0	—	—
Descriptions/Quality assurance	10	0	3.6
Specifications/Drawings	12	6	6.0
Test results	10	0	19.1
Journal articles	0	—	—
Photographs/Samples	6	0	2.5
Protocols	0	—	—
Total	85	21	11.9

Source: See Table X.

Table XII: Responses to requests for additional information in sample of 510(k) submissions.

Number of Requests	Number of 510(k)s	Number Found Substantially Equivalent	Percentage Found Substantially Equivalent	Days from Initial Submission to Finding of Substantial Equivalence
0	97	87	90	47.1
1	51	49	96	77.8
2	12	12	100	139.8
3 or more	2	1	50	337.0
Total	162	149	92	67
Source: See Table X.				

Table XIII: Requests for additional information and outcomes for a sample of 162 510(k) submissions.

Ninety percent of the 97 submissions that required no further information were found to be substantially equivalent, compared with 95% of the 65 submissions that required additional information. The high rate of equivalence findings for the latter group indicates that the submission of new data generally satisfied FDA's need for further information.

Review times are measured from the time of initial submission of the 510(k). For some of the submissions, FDA required further data before review of the 510(k) could be resumed. Sponsors of 65 submissions (40%) were asked for more information at least once, making a total of 85 additional submissions. Thirty-eight of these further submissions were considered to be official amendments, thus restarting the 90-day review period. The most common request for additional information concerned operations or instructions for use, and almost half of such requests were resolved by telephone (Table XII). Overall, about one-fourth of the 85 requests were resolved by telephone. Of course, requests for additional information increase the cumulative review time, as shown in Table XIII.

Summary. About 90% of our sample of 162 submissions in 1982 and 1983 resulted in findings of substantial equivalence, with an average time of 67 days. When FDA requires additional information, the review time as measured from the time of initial submission increases markedly. A higher proportion of the sample 510(k)s submitted in 1983 than of those submitted in 1982 took longer than 90 days to review.

Conclusion

The 510(k) process is clearly the method marketers prefer when bringing new devices to market—510(k)s outnumbered PMAs by nearly 58 to 1 in 1983.[6] The reason for this is that most marketers consider the 510(k) process to be easy and free of difficult problems. When appropriate, FDA also prefers to evaluate products through the 510(k) process. The advantages of the 510(k) process to both industry and FDA are clear from an examination of three statistics: cost of a submission ($11,000 for a PMA versus $500 for a 510[k]); average review time (380 days for a PMA versus 68 days for a 510[k]); and average FDA resources[7] (staff hours) required (1200 for a PMA versus 20 for a 510[k]). Consumers also benefit from the use of the 510(k) process, since useful devices reach the market sooner and at lower cost.

The key to the success of the 510(k) process is the concept of substantial equivalence. Although FDA may require such data where necessary to demonstrate substantial equivalence, the use of the substantial equivalence concept usually obviates the need to develop and review large amounts of safety and effectiveness data for products that clearly do not involve any significant risks or for minor changes to existing products.

Notes

1. Tucker SA, and Blozan C, "PMA Applications for Postamendment Devices: A Look at the Current Process," *Med Dev Diag Ind*, 7(6):86–94, 1985.
2. Every manufacturer, initial importer, and repackager of medical devices is required to "list"—i.e., to identify to FDA—the device types that it markets. In early 1980, the authors created a data base using the then Bureau of Medical Devices' registration, listing, and device classification files. This data base was used to produce several baseline studies, and it serves as the baseline for this analysis as well. As of early 1980, somewhat over 60% of all registered establishments had listed their device types.
3. Of a total of 174 510(k)s selected at random from 1982 and 1983 submissions (a 2% sample), 162 were logged out and were therefore usable in this and subsequent analyses of 510(k) submissions.
4. See note 1.
5. See note 1.
6. Eighty PMAs were submitted in 1983. (See note 1; also, 4616 510[k]s, this report.)
7. CDRH estimates, April 1985. □

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INTRODUCTION

The United States Food and Drug Administration develops and administers regulations under authority granted by laws passed by Congress that apply to food, drugs, cosmetics, biologics, radiation-emitting electronic products, and medical devices. Of the fourteen laws currently administered by FDA, three directly address the labeling of medical devices:

- o **The Food, Drug, and Cosmetic (FD&C) Act** - The FD&C Act applies to food, drugs, cosmetics, biologics, and medical devices. Section 201 defines the terms "label" and "labeling" as they apply to medical devices and draws a distinction between these terms. Section 502(f)(1) and (2) requires that device labeling bear adequate directions for use, operating and servicing instructions, and either adequate warnings against dangerous uses to health, or information necessary for the protection of users.

- o **The Fair Packaging and Labeling Act (FPLA)** - Because medical devices had previously been defined and regulated by the FD&C Act, Section 5 of the subsequently implemented FPLA Act refers to and makes use of the terms "label" and "labeling." Requirements of the FPLA apply to over-the-counter medical devices distributed by retail outlets.

- o **The Radiation Control for Health and Safety Act (RCHSA)** - Section 358(h) of the RCHSA requires manufacturers or distributors of radiation-emitting electronic products, including medical devices, to place certification labeling on their devices.

The specific requirements of the above laws are implemented by the Secretary of the Department of Health and Human Services (DHHS) in the form of regulations. Initially, FDA which is a part of DHHS, drafts proposed regulations. These proposed regulations are then submitted by the Commissioner of the FDA to the Office of Management and Budget. After the required time frames for public comment have elapsed, these regulations are redrafted or resubmitted, and may eventually result in finalized labeling regulations. Final regulations are published in the FEDERAL REGISTER (FR) and have the force of law.

Labeling regulations promulgated under the above Acts which pertain to medical devices are currently found in the following Parts of Title 21 of the Code of Federal Regulations (CFR).

- o General Device Labeling - 21 CFR PART 801
- o In Vitro Diagnostic Products - 21 CFR PART 809
- o Investigational Device Exemptions - 21 CFR PART 812
- o Good Manufacturing Practices - 21 CFR PART 820
- o General Electronic Products - 21 CFR PART 1010

Each of these parts or categories will be covered in detail in following sections of this chapter; however, before continuing, a few brief concepts and definitions from each Act applicable to labeling are discussed.

The FD&C Act is the primary law under which the FDA takes action against regulated products. Specifically:

- o Sections 201(k) through 201(m) of the FD&C Act address labeling "definitions."

- Sections within Chapter III of the FD&C Act address prohibited acts with respect to food, drugs, cosmetics, and medical devices. These prohibitions deal with two major areas: **"adulteration"** and **"misbranding."**
- Sections within Chapter V of the FD&C Act set forth specific instances whereby drugs or devices will be considered to be adulterated or misbranded by the FDA. The Radiation Control for Health and Safety Act applies both to medical and other radiation-emitting electronic devices. Labeling regulations based on this law pertain to FDA certification of electronic products and are found under 21 CFR Part 1010.

The medical aspects of the FPLA apply only to medical devices intended for sale to consumers from retail outlets. This Act refers to many sections of the FD&C Act. Labeling regulations based on the FPLA are found under 21 CFR Part 801.

The RCHSA applies both to medical and other radiation-emitting electronic devices. Labeling regulations based on this law pertain to FDA certification of electronic products and are found under 21 CFR Part 1010.

Labels and Labeling

Section 201 of the FD&C Act distinguishes between label and labeling. Certain provisions in Chapter V of the FD&C Act apply specifically to the "label" of the device, others are related to its "labeling." These terms are related, but not interchangeable. Of the two, the term "label" is more restricted. Generally, it consists of that part of the display confined to the device itself. On the other hand, "labeling" deals with the label on the device, and descriptive and informational literature that accompanies the device.

Section 201(k) defines "label" as a:

- "display of written, printed, or graphic matter upon the immediate container of any article..."

The term "immediate container" does not include package liners. Any word, statement, or other information appearing on the immediate container must also appear "on the outside container or wrapper, if any there be, of the retail package of such article, or is easily legible through the outside container or wrapper."

Section 201(m) defines "labeling" as:

- "all labels and other written, printed, or graphic matter
  (1) upon any article or any of its containers or wrappers, or
  (2) accompanying such article" at any time while a device is held for sale after shipment or delivery for shipment in interstate commerce.

The term "accompanying" is interpreted liberally to mean more than physical association with the product. It extends to posters, tags, pamphlets, circulars, booklets, brochures, instruction books, direction sheets, fillers, etc. "Accompanying" also includes labeling that is brought together with the device after shipment or delivery for shipment in interstate commerce.

Labeling and advertising

The distinction between labeling and advertising, both of which draw attention to the article to be sold, is often superficial or nebulous. Both are used for a similar purpose, i.e., to provide information about the product. Thus, according to an appellate court decision: "Most, if not all advertising, is labeling. The term 'labeling' is defined in the FD&C Act as including all printed matter accompanying any article. Congress did not, and we cannot, exclude from the definition printed matter which constitutes advertising."

Misbranding

Section 502 of the FD&C Act contains provisions on misbranding and false or misleading labeling. Specific requirements and exemptions are contained in regulations promulgated under this Act as will be discussed in forthcoming sections in this chapter. A device is misbranded if:

- Its labeling is false or misleading in any particular;
- It is in package form and its label fails to contain the name and place of business of the manufacturer, packer, or distributor; and an accurate statement of the quantity of the contents in terms of weight, measure, or numerical count;
- Any required wording is not prominently displayed as compared with other wording on the device, or is not clearly stated;
- Its label does not bear adequate directions for use including warnings against use in certain pathological conditions; or by children where its use may be dangerous to health; or against unsafe dosage, or methods, or duration of administration or application;
- It is dangerous to health when used in the dosage or manner or with the frequency or duration prescribed, recommended or suggested in the labeling; or
- It does not comply with the color additives provisions listed under Section 706 of the Act.

Sections 502 and 706 of the FD&C Act predate the medical device amendments and apply equally to food, drug, cosmetic, veterinary drugs, and biologics. The Medical Device Amendments of 1976 provided new authority for dealing specifically with the misbranding of medical devices. These additional provisions listed below state under what further circumstances a device is misbranded.

- If the device's established name (if it has one), its name in an official compendium, or any common or usual name is not prominently printed in type at least half as large as that used for any proprietary name;
- If the device is subject to a performance standard and it does not bear the labeling prescribed in that standard;
- If there is a failure or refusal to comply with any requirement prescribed under the FD&C Act, Section 518 on notification and other remedies, or failure to furnish any materials or information requested by or under Section 519 on reports and records; or

- If it has any representation that creates an impression of official approval because of the possession by the firm of an FDA registration or premarket notification number.

False or Misleading Labeling

Section 502(a) declares that a drug or device is misbranded if its labeling proves false or misleading in any particular. The phrase "false or misleading" is not confined in meaning to untrue, forged, fraudulent, or deceptive. In fact, the word, statement, or illustration may be true in the strict sense of the word; however, the labeling can be deemed by the FDA to be in violation of the law if it proves deceptive to the customer. It is not a necessary condition that the labeling should be flatly and baldly false; the word "misleading" in the Act means that labeling is deceptive if it is such as to create or lead to a false impression in the mind of the reader. A "false impression" may result not only from a false or deceptive statement, but may also be instilled in the mind of the purchaser by ambiguity or misdirection. It may also be caused by failure to inform the consumer of facts that are relevant to those statements actually made. In other words, the label that remains silent as to certain consequences may be as deceptive as the label that contains extravagant claims.

A device can be misbranded by making reference to a medical device registration, or a 510(k) premarket notification number assigned by FDA in response to a firm's filing requirements under the FD&C Act. Section 807.39 of 21 CFR, **Misbranding by reference to establishment registration or registration number**, and 807.97 of 21 CFR, **Misbranding by reference to premarket notification**, state that the assigned numbers do not constitute official FDA approval of the device. Additionally, any representation that connotes FDA approval as a result of complying with the device regulations is misleading and constitutes misbranding.

Similiarly, a device can be misbranded by reference to an Investigational Device Exemption (IDE) or Premarket Approval (PMA). Section 301(l) prohibits the use on labeling of any device, or in any advertising relating to such device, of any representation or suggestion or approval of an application with respect to such device is in effect under Section 515, **IDE** or Section 520(g), **PMA**.

Examples of false representations are:

- incorrect, inadequate or incomplete identification;
- unsubstantiated claims of therapeutic value;
- inaccuracies concerning condition, state, treatment, size, shape or style;
- substitution of parts or material; and
- use of the prefix "U.S." or other similar indication suggesting Government or Agency approval or endorsement of the product.

Examples of misleading labeling include:

- ambiguity, half-truths, and trade puffery;
- expressions of opinion or subjective statements; and

- failure to reveal material facts, consequences that may result from use, or the existence of difference of opinion.

Examples of other objectionable labeling practices include:

- deceptive pictorial matter;
- misleading testimonials;
- misleading list of parts or components; and
- use of brand or trade names instead of "established names."

GENERAL DEVICE LABELING

Introduction

The general labeling requirements for medical devices are contained in 21 CFR Part 801. These regulations specify the minimum requirements for all devices. Later sections in this chapter discuss any additional requirements needed for specific categories of devices.

General Labeling Provisions

Name and Place of Business (801.1)

- The label of a device shall contain the name and place of business of manufacturer, packer, or distributor including the street address, city, state, and zip code.

- If the firm's street address is in the local telephone directory, the street address can be omitted.

- If the firm listed on the label is not the manufacturer, the firm information must be qualified by an appropriate statement such as, "Manufactured for..." or "Distributed by...."

Intended Use (801.4)

- If a packer, distributor, or seller intends a device for uses other than those intended by the person from whom he received the device, these parties must furnish adequate labeling in accordance with the new intended use.

- If a manufacturer knows or has information indicating that his device is to be used [illegible] conditions or purposes other than which it was intended, he is required to provide adequate labeling in accordance with such other uses. (An example of this might be a manufacturer of dental X-ray equipment who is routinely selling his product to podiatrists.)

Adequate Directions (801.5)

- "Adequate directions for use" means directions under which the **layman** can use a device **safely** and for the purposes intended. This includes:

    - Statements of all purposes for which and conditions under which the device can be used;

- Quantity of dose for each use and usual quantities for persons of different ages and physical conditions;
- Frequency of administration;
- Duration of application;
- Time of administration in relation to other factors;
- Route or method of application; and
- Any preparation necessary for use.

False or Misleading Statements (801.6)

- o A device is misbranded if it makes a false or misleading statement with respect to another device, drug, food, or cosmetic.

Prominence of Statements (801.15)

- o A word, statement or other required information may lack the required prominence and conspicuousness for the following reasons:
  - If it fails to appear on the part or panel that is displayed under customary conditions of purchase;
  - If the package contains sufficient space and the required information fails to appear on two or more panels, each of which is designed to render it to be displayed under customary conditions of purchase;
  - Failure to extend required labeling over package space provided;
  - Lack of sufficient label space for required labeling due to placement of non-required labeling on the package; or
  - Smallness or style of type, insufficient contrast between labeling and package background, designs which obscure labeling, or overcrowding of labeling which renders it unreadable.
- o Exemptions may be granted in those instances where device labeling lacks sufficient space for required labeling provided that:
  - Existing label space is not taken up by including non-required information or by giving prominence to a portion of the required labeling; and
  - Existing label space is not used for any representations in a foreign language.
- o All labeling shall be in English with the exception of products distributed **solely** within Puerto Rico or a U.S. territory where the predominant language is other than English. In these instances the predominant language may be substituted for English.
  - If any representation on the device label or labeling appears in a foreign language, then all required labeling shall also appear in that foreign language.

Labeling Requirements for Over-the-Counter (Non-Prescription) Devices

Principal Display Panel (801.60)

- The principal display panel is that portion of the label which is intended to be displayed, presented, shown, or examined under customary conditions for retail sales. The area of the principal display panel is considered to be:
  - In the case of a rectangular package, the height x width of one side;
  - In the case of a cylindrical or nearly cylindrical package, 40% of height x circumference; or
  - In the case of any other shapes, 40% of the total surface area of the container, unless a more prominent site exists.

Statement of Identity (801.61)

- The statement of identity of the device must be listed on the principal display panel.
  - It must list the common name of the device followed by a statement of its principal intended action(s);
  - Indications for use must be listed in the directions for use; and
  - The statement must be in bold type, reasonably related in size to the most prominent printed matter on the display panel, and must be in lines generally parallel to the base of the package on which it rests.

Net Quantity of Contents Statement (801.62)

- The label of an over-the-counter (OTC) device in package form must contain a statement of net quantity of contents in terms of weight, measure, numerical count; or a combination of numerical count and weight, measure, or size, which are described below:
  - Count - If the declaration by count does not give accurate information as to the quantity, it shall be augmented by statements of weight, measure, or size;
  - Measure - In cases of established customer usage and trade custom where units of linear measure or measure of area are used, they shall be augmented when necessary with statements of weight measure or size. Liquid measure is to be expressed in terms of the U.S. gallon of 231 cu. in. and quart, pint, and fluid ounce subdivisions, and shall express the volume at 68 degrees Farenheit; and
  - Weight - Terms of weight are to be expressed in avoirdupois pound and ounce. Units of metric weight or measure are considered supplemental. The declaration may contain common or decimal fractions. Common fractions shall be reduced to their lowest terms.

  - Placement - The declaration shall appear as a separate item on each principal display panel; and be separated by at least a space equal to the height of the lettering used in the declaration, from other information appearing above and below, and separated by at least twice the width of the letter "N" from labeling to the left or right.

- o The height, ratio, and placement of lettering required on the principal display panel are a function of a number of variables related to package size, shape, composition, and the method of affixing the required labeling. This is described in detail under 21 CFR 801.62 (g) to (k).

Exemptions from Adequate Directions for Use

Prescription Device (801.109)

- o A device which, because of any potentiality for harmful effect, or the supervision of the method of its use, or the collateral measures necessary to its use is not safe unless under a practitioner licensed by law to direct use of this device, and hence for which "adequate directions for use" cannot be written, is exempt from such provided:
  - It is in the possession of either a licensed practitioner or persons lawfully engaged in the manufacture or distribution of the product;
  - Its labeling bears an Rx statement, i.e., "Caution: Federal law restricts this device to sale by or on the order of a ____(insert name of physician, dentist, or other licensed practitioner)____;"
  - Its labeling bears information for use including, indications, effects, routes, methods, and frequency and duration of administration, and any relevant hazards, contraindications, side effects, and precautions under which the device can safely be used; and
  - All labeling other than labels and cartons bears the date of issuance or date of the latest revision.

Retail Exemption (801.110)

- o A device which is delivered to the ultimate user by a licensed practitioner in the course of his practice or upon prescription are required only to bear the name and address of the practitioner, directions for use, and any required cautionary statements.

Commonly Known Directions (801.116)

- o A device is exempt from adequate directions for use if adequate directions for common uses are known to the ordinary individual.

In Vitro Diagnostics (801.119)

- o Are exempt from adequate directions for use provided that they meet those requirements found in 809.10 (covered in the "In Vitro Diagnostic Product Labeling" section of this chapter).

Medical Devices Used in Manufacturing (801.122)

- Devices used for processing, repacking, or manufacturing of another drug or device are exempt from adequate directions for use if they bear the statement: "Caution: For manufacturing, processing, or repacking."

Medical Devices Used in Teaching, Research, or Law Enforcement (801.125)

- Devices for use in teaching, law enforcement, research, and analysis are exempt if the device is shipped or sold to, or in the possession of, persons lawfully engaged in instruction in pharmacy, chemistry, or medicine (not involving clinical use), law enforcement, or chemical analysis or physical testing.

Expiration of Exemptions (801.127)

- Exemptions from adequate directions for use are terminated:
    - If devices are shipped to individuals other than those who are listed as exempt, or
    - If the devices are used for other than the exempted purposes.

Other Exemptions

Exemptions from Packaging and Labeling Requirements (801.150)

- In-process devices that are being transported (in transit) from one manufacturing site to another are exempt if:
    - The person who introduced the product into commerce is the owner of the firm where the device is to be further processed.
    - The person introducing the product into commerce is not the owner, and the delivery is to be made under a written agreement which includes the names and addresses of the firms and listing those specifications necessary for further processing.
    - The shipments are unsterile devices, are labeled as sterile, are in transit to a contract sterilizer [801.150(e)], and are exempt only if both of the following are met:
        1) There is in effect a written agreement between the two parties containing:
            i. names and addresses of both parties which is signed by both the person authorizing the shipment and the person in charge of the sterilization facility;
            ii. instructions for maintaining records to assure total accountability;
            iii. acknowledgment that the devices are nonsterile and being shipped for further processing;
            iv. a statement detailing the sterilization process, sterilant media, equipment, and quality assurance controls to be used; and

2) Each pallet, carton, or other designated unit is conspicuously marked to indicate its nonsterile nature.

This exemption is void if the product is adulterated or misbranded, or if a copy of the agreement is not available for FDA inspection.

Labeling Requirements for Specific Devices

Warning and Caution Statements (801.403)

- This part contains recommended or suggested wording for warning and caution statements for the following devices:
  - Denture reliners, pads and cushions
  - Denture repair kits
  - Infrared generators (including heating pads)
  - Insulin syringes
  - Mechanical massagers and vibrators
  - Steam or turkish bath
  - Ultraviolet generators

Use Related Statements (801.405 to 801.430 as listed below)

- Certain devices require specific labeling which may include not only package labeling, but informational literature, patient release forms, performance testing, and/or specific tolerances or prohibitions on certain ingredients. The following devices have additional labeling requirements:
  - Denture repair or refitting kits (801.405)
    Special labeling and directions are listed in this section.
  - Pessaries for intracervical and intrauterine use (801.408)
    This section specifies that stem types and wing-tip types are considered dangerous and thus automatically misbranded. Hollow tube types are permitted, but require a Rx legend.
  - Impact resistant lenses in sunglasses and eyeglasses (801.410)
    This section specifies that case hardening of glass lenses, statistical testing of plastic lenses, "drop ball" testing, and documentation of these activities are required.
  - Ozone emission levels (801.415)
    This section specifies that ozone emission is restricted to levels below 0.05 parts per million in certain devices, and not permitted at all for use in any medical conditions for which there is no proof of safety or efficacy.
  - Chlorofluorocarbon propellants (801.417)
    This section specifies the use is prohibited except for use in contraceptive foams and certain metered drug dosage forms as detailed under 21 CFR 2.125. Special labeling is required on devices using this propellant as listed under 801.425.

- Hearing aids (801.420)
  Labeling requirements related to warnings, directions to dispensers and users, and technical data are contained in this section. Conditions for sale requirements related to availability of instructional brochures, patient waivers, and recordkeeping requirements are contained in 801.421.

- Intrauterine contraceptives (801.427)
  Professional and patient labeling requirements related to description, indications, precautions, and warnings are contained in this section.

- Menstrual tampons (801.430)
  This section contains those labeling requirements related to Toxic Shock Syndrome (TSS) information, warnings, and advisories.

IN VITRO DIAGNOSTIC PRODUCT LABELING

Introduction

In vitro diagnostic products (IVD's) are those **reagents, instruments, and systems** intended for use in diagnosis of disease or other conditions, including a determination of the state of health, in order to cure, mitigate, treat, or prevent disease or its sequelae. Such products are intended for use in the collection, preparation, and examination of specimens taken from the human body. In vitro diagnostic (IVD) labeling requirements are located in 21 CFR Part 809. Numbers appearing in parentheses next to subject headings are the corresponding sections of 21 CFR. This section contains the basic requirements for label and labeling (package insert) as specified in the labeling regulations for in vitro diagnostic products.

Specific information on the development and drafting of labels and labeling is contained in the "Development of Device Labeling" section in this chapter.

Label Requirements for the Immediate Container [809.10(a)]

The label for IVD's must state the following information, except in cases where it is not applicable. In addition, all information must appear on the outside container or wrapper, or be easily legible through the outside container or wrapper.

If the presence of any label information will interfere with the test, the information may appear on the outside wrapper or container instead of the label.

If the immediate containers are too small, or otherwise unable to bear labels with sufficient space, then the required labeling as listed below annotated with an asterisk (*) may appear on the outer container **labeling** only.

Label requirements are as follows:

o The established and proprietary names of the product, e.g., cholestrolometers;

* o The intended use or uses, e.g., pregnancy detection, diabetes screening, etc.;

* o A statement of warnings or precautions for users listed in 16 CFR part 1500 (hazardous substances) and any other warnings appropriate to user hazards, and a statement "For In Vitro Diagnostic Use;"

- o Name and place of business of the manufacturer. packer. or distributor:
- o Lot or control number traceable to the production history
  - Multiple unit products must have traceability of the individual units;
  - Instrument lot numbers must allow for traceability of subassemblies: and
  - A multiple unit product that requires use of its components as a system should have the same lot number. or other suitable uniform identification. on all units.

* o For **Reagents:**

- Established (common or usual) name:
- Quantity. proportion. or concentration of all active ingredients: e.g.. mg.. weight per unit volume. mg./dl etc.. and for reagents derived from biological materials the source and measure of its activity. e.g.. bovine. I.U.. etc.:
- Storage instructions. i.e.. temperature. humidity. etc.:
- Instructions for manipulation of products requiring mixing or reconstitution:
- Means to assure that the product meets appropriate standards of purity. quality. etc.. at the time of use. including one or more of the following:

i. expiration date (date beyond which the product is not to be used):

* ii statement of any visual indication of alteration:

* iii. instructions for a simple check to assure product usefulness;

* - The net quantity of contents.

Labeling Requirements for Inserts and Outer Packaging [809.10(b)]

Labeling must contain in one place the following information in the FORMAT and ORDER listed below. except where information is not applicable. or as specified in a standard for a particular product class.

If the device is a reagent intended as a replacement in a diagnostic system. labeling may be limited to that information necessary to adequately identify the reagent and to describe its use in the system.

If the device is a multiple purpose instrument used for diagnostic purposes. and not committed to specific diagnostic procedures or systems. labeling can be restricted to those points annotated by an asterisk (*).

* o The proprietary and established product name:

* o The intended use of the product and whether it is a qualitative or quantitative type of procedure. e.g.. screening. physician's office. home use. etc.:

- o Summary and explanation of the test, including a short history containing methodology and the special merits and limitations of the test;

- o The chemical, physical, physiological, or biological principles of the procedure.

- o For **Reagents**:

  - The common name, if any, and quantity, proportion, or concentration or each reactive ingredient; and for biological material, the source and measure of its activity;

  - Appropriate cautions or warnings listed in 16 CFR Part 1500; the statement: "For In Vitro Diagnostic Use;" and any other limiting statements appropriate to the intended use of the product;

  - Adequate directions for reconstitution, mixing, dilution, etc.;

  - Appropriate storage instructions;

  - A statement of purification or treatment required for use; and

  - Physical, biological, or chemical indications of instability or deterioration.

* o For **Instruments**:

  - Use or function;
  - Installation procedures and requirements;
  - Principles of operation;
  - Performance characteristics and specifications;
  - Operating instructions;
  - Calibration procedures, including equipment and/or materials;
  - Operational precautions and limitations;
  - Hazards; and
  - Service and maintenance information.

- o Specimen collection and preparation for analysis, describing:

  - Special precautions/preparations;
  - Additives necessary to maintain specimen integrity;
  - Known interfering substances; and
  - Recommended specimen storage, handling, and shipping instructions.

- o A step by step outline of recommended procedures from the reception of the specimen to the obtaining of results. In addition to the following, this should include a list of any points that might improve precision or accuracy;

  - A list of materials provided and instruction for use, e.g., reagents, equipment, etc.;

  - A list of necessary materials that are not provided (include details such as sizes, numbers, types, and quality);

  - A description of the amounts of reagents necessary, and parameters such as time, temperature, etc.;

    - A statement related to final reaction stability and any time restrictions on accurate measurements;
    - Details of calibration, identifying and listing any necessary preparation of the reference materials, samples, and blanks. Describe the calibration range including the highest and lowest values measured; and
    - Details of necessary quality control procedures and materials, e.g., positive and negative controls, acceptable performance limits.

- o Explanation of the procedure for calculating the unknown, including the definition of each component of the formula, a sample calculation, and the number of significant figures appropriate for the answer;
- o Limitations of the procedure, e.g., identify situations which will have an adverse impact on test results;
- o Expected values including the range and how it was established;
- o Specific performance characteristics as appropriate including accuracy, specificity, precision, and sensitivity;
- * o Bibliography;
- * o Name and place of business of the manufacturer, packer, or distributor; and
- * o Date of issuance of the last labeling revision by the firm.

Exemptions from Labeling Requirements

Shipments or other deliveries of IVD devices are exempt from label and labeling requirements in the above headings and from standards listed under Part 861 provided the following conditions are met:

- o A shipment or delivery for an investigation subject to Part 812, Investigational Device Exemption (IDE), if the device is in compliance with the subject IDE; **or**
- o A shipment or delivery for an investigation that is **not** in compliance with Part 812 (most IVD's are exempt from the IDE because of the following labeling) if the following conditions are met:
    - A product in the laboratory research phase, not represented as an IVD, that is prominently labeled: "For Research Use Only. Not for use in diagnostic procedures;" and
    - A product that is being shipped or delivered for product testing prior to full commercial marketing that is prominently labeled: "For Investigational Use Only. The performance characteristics of this product have not been established."

Labeling of General Purpose Laboratory Reagents and Equipment

General purpose items include routine laboratory reagents such as hydrochloric acid and equipment such as glassware whose uses are generally known by persons trained in their use. They do not need to bear the directions for use listed under **Label Requirements for the Immediate Container** and **Labeling Requirements for Inserts and Outer Packaging**. if their labeling meets the requirements listed below. If the product packaging is too small to accommodate a label with sufficient space for the labeling. and if the product is packaged in an outer container which has all of the following on its **labeling,** then only those portions annotated with an asterisk (*) must be on the product **label**.

o **Reagents**:

* - The proprietary and established name;

- A declaration of the established name. if any. and quantity. proportion. or concentration of the reagent ingredient stated in a system generally recognized by the user;

- A statement of the purity and quality including a qualitative statement of any impurities. This can be satisfied by using a statement of conformity with a generally recognized and available standard;

- A statement of warnings or precautions for users as contained in the regulations in 16 CFR Part 1500 and any other appropriate warnings. and the statement: "For Laboratory Use;"

- Net quantity of contents in terms of weight or volume. or numerical count. or any combination thereof;

- Appropriate storage instructions;

* - Name and place of business of the manufacturer. packer. or distributor; and

* - A lot or control number traceable to the manufacturing history of the product.

o **Equipment**

- Product labeling need include only a statement adequately describing the product. its composition. and physical characteristics if necessary for its proper use.

LABELING FOR INVESTIGATIONAL AND 510(K) DEVICES

Introduction

An "investigational device" is a device that is the object of a clinical investigation or research involving one or more human subjects to determine its safety and effectiveness. This definition also includes "transitional devices" which are devices that had been previously regulated by the FDA as drugs prior to the passage of the Medical Device Amendments. for example. pregnancy test kits.

All newly registered medical device establishments and existing medical device firms introducing new or significantly modified devices must notify FDA of their intent to market the device at least 90 days before introducing the devices into commercial distribution. This is done via a 510(k) Premarket Notification submission which is required by that corresponding section of the FD&C Act. The purpose of this submission, which includes copies of proposed device labeling, is so that FDA can determine whether or not the device as labeled is substantially equivalent to one that was in commercial distribution prior to May 28, 1976. This includes Class I, II, and III devices, or a device that was placed onto the market after that date that was classified by FDA as Class I or Class II. The 510(k) process does not require manufacturers to demonstrate that their devices are identical to marketed devices; only that the devices and their labeled uses be substantially equivalent in terms of safety and effectiveness. Clinical data may be required before FDA can determine whether a device is substantially equivalent under a 510(k).

If a device is found by the FDA to be not substantially equivalent and placed into Class III, the firm must demonstrate proof of safety and efficacy to FDA prior to marketing. This demonstration is done via a Premarket Approval application (PMA). The PMA must contain data which show the device to be safe and effective. An approved Investigational Device Exemption (IDE) enables a device to be shipped to researchers in order to collect data before the device is cleared by FDA for commercial distribution.

FDA must approve IDE applications for significant risk devices. Non significant risk devices are subject only to Institutional Review Board (IRB) approval. The IDE exempts device sponsors and investigators from certain regulatory requirements, i.e., those related to: performance standards, misbranding, premarket approval, registration, and listing, for the duration of the study. The IDE application will contain an investigational protocol which details the nature of the study, and the nature of the data to be obtained and furnished to FDA as proof of safety and efficacy. The sponsor provides detailed information on device labeling in the investigational plan. This information may vary depending on the device and the nature of the study, and can extend to such items as any advertisements placed in order to recruit human subjects for the investigation.

Premarket Notification [510(k)] Labeling

There is no application form, but there is a format for the 510(k) submission contained in 21 CFR 807.81 to 807.97. Information required in the submission includes: a description of the device and its specifications, the class into which the device has been placed by FDA, the firm's registration number, a statement comparing the device to others of comparable type, and copies of labeling and promotional literature. The proposed device labeling submitted in the 510(k) plays an important role

Labeling information to be included in a 510(k) submission may include:

- device labels;
- packaging labeling;
- special handling or storage conditions;
- instructions and/or instruction manuals;
- service manuals;
- promotional literature such as advertisements, publications, etc.; and
- other labeling requirements such as UL, F.C.C., etc.

If the device labeling makes new, previously unsubstantiated claims or promotes use of the device for purposes or conditions other than currently marketed similar devices, the FDA would most likely place the device into Class III and it would need premarket approval prior to marketing. In those instances where a device is substantially equivalent to an existing device, or technology currently in use, a firm should attempt to obtain 510(k) clearance rather than go for premarket approval. The savings in time and cost could be considerable.

IDE Device Labeling Requirements (21 CFR Part 812.5)

If a device is found by the FDA to be not substantially equivalent and placed into Class III, the firm must submit a PMA to FDA prior to marketing to demonstrate proof of safety and efficacy. The firm must first apply for an Investigational Device Exemption (IDE) to exempt them from certain regulatory requirements for the duration of the study. The IDE application will contain an investigational protocol which details the nature of the study, and the nature of the data to be obtained and furnished to FDA as proof of safety and efficacy. The firm provides detailed information on device labeling in the investigational protocol. This information may vary depending on the device and the nature of the study, and can extend to such items as any advertisements placed in order to recruit human subjects for the investigation. For example, product labeling should be sufficient to insure stability of the test article for the duration of the study (storage requirements, recalibration procedures), bear sufficient directions for proper administration, alert the user of the investigational status of the article, and detail procedures to follow in the event of patient injury.

In addition to any labeling requirements specified in the IDE study protocol, the following general labeling is required:

- o Information required in 801.1, i.e., name and place of business of the firm, quantity, and in 801.109, the following statement: "CAUTION: Investigational Device. Limited by Federal (or United States) law to investigational use."
- o A description of all relevant contraindications, hazards, adverse effects, interfering substances or devices, warnings and precautions.
- o Absence of any statements that are false or misleading, or that represent the device as safe and effective for its investigational purpose.
- o Any device shipped solely for use on laboratory animals must be labeled: "CAUTION - Device for investigational use in laboratory animals or other tests that do not involve human subjects."

GOOD MANUFACTURING PRACTICE LABELING REQUIREMENTS

Introduction

Medical device manufacturers must incorporate in their quality assurance (QA) program several elements that relate to labeling in order to meet the requirements of the GMP regulation. The QA program must be adequate to assure that labeling meets the GMP device master record requirements with respect to legibility, adhesion, etc., and assure that labeling operations are controlled so that correct labeling is always issued and used.

Because many activities must be performed and controlled during the development and use of labeling, Table 5.1 is presented as a checklist. It contains a typical sequence of events required to develop and control labeling.

Labeling includes equipment labels, control labels, package labels, directions for use, maintenance manuals, etc. The displays on CRT's and other electronic message panels are considered labeling if instructions, prompts, cautions, and parameter identification information are given.

Various sections of the GMP regulation have an impact on labeling: Section 820.20(a)(2) requires approval or rejection of packaging materials and labeling; and Section 820.40 requires buildings to be of suitable design and have sufficient space for packaging and labeling operations. Section 820.120 deals with specific requirements for the design and control of labeling. It applies to the design application of labeling to assure legibility under normal conditions of use over the expected life of the device; and also to inspection, handling, storage, and distribution of labeling. FDA considers a device to be adulterated if these requirements are not met. These requirements do not apply to the adequacy of labeling content, except to make sure the content meets the labeling specifications contained in the device master record. However, failure to comply with GMP requirements such as proofreading and change control could result in labeling content errors. In such cases, the device is misbranded and adulterated. Labeling content is covered in the section on "Development of Labeling."

Specifications are required in the device master record (820.181, 182) for the content and physical design parameters of labels. Labeling specifications are: engineering drawing and/or artwork for each label, appropriate inspection or control procedures, and appropriate procedures for attaching the labels. All procedures, drawings, and artwork must have the name of the preparer, an approval signature, and a date. The approval signature, date, etc., may be on the backside of artwork or on a label approval form. Further, artwork may contain only an identification code or title if the "content" of the artwork is duplicated on approved engineering drawings or adequately identified (cross-referenced) with respect to the label approval form.

Hardcopy labels, package inserts, and similar labeling are specified and purchased as components. For correct purchase and use of labeling, specifications are usually stated on engineering drawings and/or purchase specifications. Thus, artwork or "copy" alone will not fulfill the device master record requirements for labeling except for the most simplistic labeling such as brief errata sheets.

The engineering drawings or purchase specifications and mounting procedure must specify, as appropriate, the label substrate, dimensions, ink, finish, mounting method, etc., so that the purchased label will remain attached and legible during the customary conditions of processing, storage, handling, distribution, and use.

Front panels, other instrument panels, meters, fuses, pushbuttons, and the like often are labels or contain labels and must, as appropriate, meet GMP master record and control requirements. Component specifications, assembly drawings, and test/inspection procedures are appropriate GMP controls to prevent mixup of meters, pushbuttons, and other labeled instrument controls. Controls to prevent mixups are generally not needed for front and other instrument panels.

Whether a firm considers a software driven display to be labeling or data makes little difference under the GMP regulation, because either way, the finished device labeling or data must meet the device master record specifications. When firms develop and validate

TYPICAL SEQUENCE OF THE GMP CONTROL OF LABELS (TABLE 5.1)

PHASE	DEVICE TYPE		GMP SECTION (PART 820.)	CONTROL ACTIVITY
1. Development	NC*	C*	.120 & .100	Text review. Quality of mounting (rivets, adhesives, etc.). Quality of ink, anodize, etc. Content per 21 CFR 801, 807, 809, company claims and standards.
2. Evaluation	NC	C	.120	Simulated or actual processing (e.g., Sterilization), shipping tests, etc.
3. Documentation	NC	C	.181	Approve, date and change control label drawings.
		C	.121a	A key label must contain control number of finished device.
4. File Sample		C	.182b	Copy of actual label or artwork in the master record. See .181.
5. Procurement	NC	C	.120a	Proofread before release to inventory stock.
		C	.121b	Record signature of proofreader and date.
6. Storage	NC	C	.120d	Store labels so as to prevent mixups.
		C	.121c	Restrict access to labels to authorized persons.
7. Separate Operations	NC	C	.120b	Separate multiple operations to prevent mixups.
8. Area Inspection	NC	C	.120c	Before beginning labeling operations, designee to inspect area & remove extraneous devices & labels.
9. Issuance	NC	C	.120e	Examine for identity and, where appropriate, expiration date and control number. Record date and person examining labels.
10. Inspection	NC	C	.160	Inspect finished device per written procedure.
		C	.161	Designee must check all acceptance records & test results & see that records are present and complete.

* NC = Noncritical; C = Critical

software, they should also review these electronic displays to see that the "labeling" meets all applicable requirements, such as adherence to specifications in the master record, correct parameter identification, agreement with the instruction manual, and, of course, correct display of performance data.

When reviewing or auditing labeling operations, it is wise to keep in mind that the GMP regulation contains flexible requirements and thus allows flexibility in a quality assurance program. The degree of labeling control needed to satisfy the GMP regulation varies considerably for different devices and operations. In order to avoid wasting money and increasing the cost of health care, manufacturers need to give considerable and prudent thought to the appropriate level of control needed for their operations as allowed by 820.5. Information and guidelines presented in this chapter should aid manufacturers in making these decisions. The level of control needed should be reconsidered when products are added or changed. Likewise, the controls needed and success of the existing control program **must** be reviewed during QA system audits.

General Device Labeling Requirements

Label integrity

All labels must be designed and applied to devices and containers so that the labels will remain in place and legible during the customary conditions of distribution, storage, and use. Likewise, other labeling such as user instructions should remain legible during customary storage and use. Note that 820.120(a) which states "Labels shall be designed, printed, and applied so as to remain legible..." refers to the actual design of the label and mounting method--not just testing or inspection of these to show that design requirements have been met. [Inspection is covered by the second sentence of 820.120(a), and by 820.120(e), 820.20(a), 820.80 and 820.160.] For example, labeling printed by machines onto plastic in vitro diagnostic media plates is sometimes smeared and thus is inadequate [FD&C 502(f)]. The manufacturers of such devices must assure that the print is legible and will remain legible until used.

Some magazines use "wet" ink which smears when touched by sweaty or oily fingers. Obviously, this type ink will not meet the GMP design requirements for package inserts, instruction manuals, etc.

Labels may be mounted by adhesives, screws, rivets, drive screws, etc., or printed or etched onto panels and/or onto controls. The labels should be located so that they will be seen but not be abraded during use. (Some of us have seen the unbelievable cases where safety labels on ladders and riding lawnmowers were placed in the foot rest areas. Of course, they were scrubbed off after a few uses!)

Receipt and inspection

Upon receipt, all packaging and labeling materials, including preprinted containers, inserts, and preprinted packaging materials must be examined and, if deemed necessary by the company, tested to assure conformance with specifications. Also, samples of labels must be proofread by a designated individual(s). After being accepted by a responsible individual, these components may be placed into inventory or into production. These inspections must be recorded in the device history record as required by 820.80(a) and 820.120 to show that inspection and proofreading were performed. The inspection record for device labeling should be kept simple.

Area separation and inspection

All labeling and packaging operations should be separated to the degree necessary (820.5 and 820.40) to **make certain** there are no mixups between similar products or labels. Separation may be either a physical or spatial separation or by performing the labeling and packaging at different times for different devices. Separation is not required when mixups are impossible such as the case of labeled front panels that only fit the intended family of instruments (devices).

The likelihood of a labeling mixup determines how stringent production area controls should be. For example, label control need not be stringent if only dissimilar products and labeling are processed. Before beginning any packaging and labeling operation in which mixup could occur, the production area and equipment for the operation **must** be thoroughly examined to make certain that any devices and labeling materials remaining from previous operations have been removed. It is important to make certain that the surrounding area, tables, packaging lines, printing machines, and other equipment are cleared of labels and other materials used in the previous operation.

Unused labeling that contains pre-coded serial numbers, manufacturing date, expiration date, control number, etc., should be destroyed and not returned to the label storage area. The GMP regulation does not require reconciliation of the number of labels used versus the number issued, although this control is recommended for some devices, such as when different sizes of the same product are being packaged or otherwise labeled.

Storage

All printed packaging and labeling materials, including preprinted containers, inserts and preprinted packaging materials, **must** be stored in an area and manner suitable to prevent mixups (820.40, 820.120). Labeling should be identified and segregated to the degree necessary to prevent mixing of similar labeling. Access to labeling should be limited to authorized personnel.

Storage control should be appropriate for the number and kind of devices. For example, a firm that manufactures only one product with one label does not need an elaborately controlled storage area. Similarly, a firm with only a few types of devices having dissimilar labeling would not normally require stringent control.

One case that requires dedicated attention to storage and control is prelabeled "sterile" but "not-yet-sterilized" devices. Firms must make **absolutely certain** that mixups cannot occur. Also **make certain** that all such samples, if used for market promotion, are sterile or stamped with a manifest caution statement because a packaged and labeled market-promotion sample might be used by the recipient. Quality awareness training is required by Section 820.25 and marketing personnel must be informed of labeling control requirements and the consequences of a violation.

Label check and record

When issued for use, labeling **must** be carefully examined to make certain the contents of the labeling comply with the labeling specifications in the device master record for the specific device being produced. This examination **must** include any control numbers or expiration dates used on the labels. A record of this issuance check, including the date and name of the person performing the examination, **must** be made in the device history record.

If used, expiration dates **must** reflect the time after final packaging during which the device is fit for its intended use when stored and used per its labeling. The manufacturer should have stability test data which establishes the interval that the device remains fit for use.

If label mixups **cannot** occur--for example, a firm makes only one device or uses only one label--and there are no control numbers or expiration dates, the original inspection when the labeling was placed into inventory is an adequate check for compliance with the master record specifications. A second check need not be performed because it serves no purpose (820.5). If, however, there is any possibility that incorrect labeling can be used, a second check **must** be made when the labeling is issued for application, packaging, or shipping.

Changes

Labeling is part of the device master record; therefore, all changes to labeling **must** be made under a formal change control system similar to that required for specifications [820.100(a)(2)]. Any changes to labeling **must** be formally reviewed and authorized before implementation.

When making changes to primary aspects of a device and to primary documentation, the review group must determine if any secondary items such as labels or instructions are affected and also need changing. There should be a check-off block on change-order forms for recording that the effect of the primary change on labeling was considered and appropriate action was taken.

Relabeling and over-labeling

Over-labeling by placing a new label over an old label is discouraged by FDA but is acceptable as long as the new label and its use meet GMP requirements (820.120, 820.115) for attachment, legibility, reprocessing, and change control. (Over-labeling is also discouraged in some foreign countries.)

Additional Labeling Requirements for Critical Devices

Labeling for critical devices **must** meet the noncritical device labeling requirements and meet the three additional requirements in 820.121 as covered below.

Control number

Critical device labeling **must** contain a control number, serial number, letters, etc., for traceability. This means a control number for the finished device, and not the label itself. Most labeling, however, also contains another number, such as a drawing number, for control of labeling configuration and procurement.

The control number for traceability need not be on every label on the device; however, the control number **must** appear on the unit label that goes to the ultimate user. The label on a shipping carton for bulk items does not meet this requirement because bulk items may go to a central distribution point in the user-facility and the shipping carton would most likely be discarded. In order to meet this traceability requirement, a label that would most likely reach the nurse or other user station **must** have the control number.

Proofreader's signature

Before releasing labeling for critical devices to inventory, samples of labeling **must** be proofread as required for noncritical devices. In addition, the signature of the proofreader and the date of the proofreading **must** be recorded in the device history record.

Access restriction

Access to labeling **must** be restricted to authorized personnel. Labeling also should be stored in an adequately segregated area to minimize the chance of mixups. Although the access requirement applies to labeling for critical devices, it is also recommended for labeling for noncritical devices because it increases the control over the label storage area with no significant increase in cost.

Sterile Device Labeling

Special attention should be given to the labeling of sterile devices. Devices that are not sterile in their entirety (for example, sterility may be needed only for the lumen of certain devices) **must** be labeled to properly inform users what is actually intended to be "sterile" in the package. For example, a possible limiting statement might be:

> "**Caution:** Only the fluid path of the set is sterile and nonpyrogenic. Do not use in a sterile or aseptic area without proper precautions."

Some devices are intended to be sterilized by the user before use. In this situation, the labeling should provide adequate information as to at least one suitable method of sterilization and any precautions or safeguards to be followed. For example, the labeling should describe any:

o special cleaning methods required;

o changes in the physical characteristics of the device that may result from reprocessing which affect its safety, effectiveness, or performance; and

o limit on the number of times resterilization and reuse can be done without affecting the safety or effectiveness of the device.

In the case of single-use sterile devices, some manufacturers include labeling to advise against resterilization and reuse. Some devices are simply not designed or constructed to be recleaned, and may not be capable of withstanding the necessary recleaning and resterilization procedures. Where reuse is common practice, manufacturers are encouraged to provide the information described in the above list.

The label of multi-device kits or packages containing a combination of sterile and nonsterile products **must** not state or imply that all contents are sterile.

The need for users to have instructions on how to open a sterile device package to avoid contamination of the device also needs to be evaluated, and when necessary, such instructions should be included in the labeling.

When a manufacturer modifies a device, the manufacturer must also review the labeling to make certain that it reflects current revisions and specifications. Some manufacturers identify labeling with a drawing number plus a revision code or date as an aid in identifying current labeling. The package insert or other labeling for in vitro diagnostic products is **required** to contain the revision date [21 CFR 809.10(b)(15)].

Shelf-life dating solely for package integrity and sterility is not usually required by FDA for general medical devices. There may be a need for expiration dating when a particular component of a device, such as a battery or diagnostic reagent, has a finite useful life. Labeling for in vitro diagnostic devices [809.10(a) and (b)] requires an expiration date or some other means by which users may be assured of quality at the time of use. This requirement applies to both sterile and nonsterile in vitro diagnostic devices.

Although not required by regulation, most manufacturers of complex devices and sterile devices voluntarily use lot or serial numbers for production control and, if the need arises, to expedite failure investigations, repairs, modifications, or recalls. Lot, batch, or other control numbers are required for:

- critical devices (820.121);
- some products subject to radiological health standards; and
- in vitro diagnostic devices [809.10(a)(9)].

Adequate labeling for a medical device requires proper design and procurement of the labels and labeling. Design includes labeling content that meets the requirement of the GMP regulation as well as the needs of the customer. To achieve these goals a number of concepts must be kept in mind such as: writing to the reader, referring to the actual device in labeling, obvious identification of the controls used, etc.

Contract Sterilization

Finished devices that are terminally sterilized by a firm other than the manufacturer pose a unique labeling problem. A common industry practice is to send the finished device in its final packaging to a contractor for sterilization. The final packaging is labeled as sterile even though the goods are unsterile during shipment from the manufacturer to the contractor. Specific restrictions apply in this instance, and a written agreement between the parties must be in effect [820.150(e)]. The requirements for the labeling of in process sterile goods in transit to the contract sterilizer are addressed in detail by Section 801.150, and covered previously under **Other Exemptions** in this booklet. Extreme care must be taken in this situation to eliminate the possibility of an unsterilized product being mistaken for a sterilized product. A firm should seriously consider the use of "visual indicator" labeling to distinguish between product before and after sterilization, e.g., the use of indicator tape with bands that develop color upon exposure to steam or ethylene oxide, or stick-on "dots" which change color upon exposure to radiation. Bear in mind that visual indicators will provide confidence that the product has been exposed to a sterilant and not that the product **is** sterile. A firm should also consider the use of dosimeters, i.e., a product that undergoes an irreversible change in physical or chemical properties that is proportional to the amount of exposure to a sterilant. Some contract sterilizers affix labeling to a contractor's product in the form of a sterilization number stamped upon the device container, or outer shipping containers. Firms who use the contract sterilizer's lot number as assurance that their devices have undergone sterilization should determine, via an audit of the facility if possible, that sterilization lot numbers are applied after, not before, being subject to sterilization.

Regulations on distribution are contained in 21 CFR 801, Subparts A and E; and GMP Sections 820.150, 820.160 and 820.161. Devices that have been sterilized, held, or shipped to the manufacturer's warehouse or other **controlled** distribution point before final release must be properly labeled. The pallets, or designated unit, must be marked to indicate the status of the device such as "sterilized: awaiting test results," or an equivalent statement. The company must be able to show that it has control of the devices until final release and, if necessary, could have them destroyed or returned for reprocessing. For this reason, a distributor's warehouse or facility is not considered a controlled distribution point.

RADIATION-EMITTING DEVICE LABELING

Introduction

Labeling of radiation-emitting products applies to medical devices; all products which emit ionizing, or nonionizing electromagnetic or particulate radiation; and products which emit sonic, infrasonic, or ultrasonic radiation as the result of operation of an electronic circuit. Radiation-emitting devices include products that emit radiation either by design (e.g., X-ray equipment) or as a consequence of operation (e.g., television set), but exclude products that emit radiation as a result of the decay of a radioactive element or isotope (e.g., an ionization type smoke detector). Section 358 of the Radiation Control for Health and Safety Act (RCHSA) of 1968 authorizes the development of Federal standards for these types of radiation producing products. These standards are contained within the regulations listed under 21 CFR Part 1000. The corresponding regulations are listed by product type in subsequent headings of this section. This booklet will cover only those portions of these standards related to product labeling and will not attempt to address technical specifications contained in the standards. Thus, the nature and placement of labeling may vary from those previously discussed under **General Device Labeling;** however, the concepts of "label" and "labeling" remain the same, e.g., the "label" of a device might consist of a warning label on the console of an X-ray system, as well as a red indicator light on the panel; the "label" of a television receiver might consist not only of the name of the manufacturer, date of manufacture, and user caution statements, but also of labels **inside** the receiver related to high voltages and X-ray shielding.

At the present time, as a matter of choice and practicality, FDA does not choose to actively regulate some common household products such as radios and incandescent light bulbs; however, if such products were found to pose a consumer hazard, the FDA could choose to regulate them. A good example of a hazard to consumers is the cordless telephone. As a result of consumer complaints, and confirmed injuries due to the placement, volume, and frequencies of ringers in certain brands of telephones, FDA set and enforced guidelines to prevent hearing injuries.

This section will cover labeling of radiation-emitting medical and other electronic devices. Due to the amount of technical data contained in the corresponding sections of the CFR, reprints of the CFR sections pertaining to laser labeling will be used where appropriate to demonstrate format requirements. Numbers appearing in parentheses next to subject headings are the corresponding sections of 21 CFR.

General Labeling Requirements for Electronic Products (1010.3)

Manufacturers of electronic products covered under a performance standard shall provide the following information on a tag or label permanently affixed or inscribed on the product. The following information should be readily viewable when the product is fully assembled:

- o The full name and address of the manufacturer of the product.
  - Alternately, the product can contain the full name and address of a company or individual other than the manufacturer, provided that the full name and address of the actual manufacturer has been previously identified to the Director of the Center for Devices and Radiological Health (CDRH). (This alternative is necessary so that CDRH can identify manufacturers of particular models of devices in those instances where the listed distributor uses different manufacturers for each model.)
  - Abbreviations such as Co., Inc., or their foreign equivalents, and the initials of the first and middle names of individuals may be used.
- o The place and month and year of manufacture.
  - The place of manufacture may be expressed in a code if the code has been previously supplied to the Director of CDRH.
  - The month and year of manufacture cannot be coded or abbreviated. The month and a four digit number for the year must appear as follows: **"MANUFACTURED: (Insert Month and Year of Manufacture)"**

In a case where it is not feasible to affix identification labeling in accordance with the above, the Director of CDRH may approve an application for an alternate means of identification.

The manufacturer must furnish the Director of CDRH with a complete listing of all brand names and the names and addresses of the individuals or companies for which electronic products are manufactured under a standard.

Electronic products intended for United States Government use may be exempted from the above upon application to the Director of CDRH by the manufacturer, assembler, or a U.S. department or agency.

All products intended solely for export shall be labeled or tagged to show that they are intended for export.

The manufacturer of any electronic product covered by an exemption from performance standards (i.e., standards, other than labeling, which are not covered in this chapter) must permanently attach a tag or label stating:

"This electronic product has been exempted from the Food and Drug Administration radiation safety performance standards prescribed in the Code of Federal Regulations, Title 21, Chapter I, Subchapter J, pursuant to Exemption No.__, Granted on ________."

Ionizing Radiation-Emitting Products

Television receivers (1020.1)

A television receiver is an electronic product designed to receive and display a television picture through broadcast, cable, or closed circuit television. Digital monitors which display a fixed (non-moving) image, e.g., computer screens, are excluded from the standard.

- Any receiver capable of producing radiation in excess of the standard through component failure or improper adjustment shall have a permanently affixed or inscribed warning label listing the high voltage specification and instructions for adjusting the high voltage to the specified value.

Cold-cathode gas discharge tubes (1020.20)

Cold-cathode discharge tubes are devices designed to demonstrate the effects of a flow of electrons or the production of X-rays.

- Manufacturers shall provide applicable safety instructions, instructions for use, and power source specifications for each tube.
  - Each enclosure or tube shall have permanently affixed polarity identification of the terminals.
  - Tubes designed for heat, fluorescence, or magnetic effect must have a warning indicating that excess power application may result in x-radiation.
  - Tubes designed for x-radiation must bear a warning that the device produces X-rays when energized.
- The required tags or labels must be visible when the device is fully assembled for use.

Diagnostic X-ray systems (1020.30)

Diagnostic X-ray systems incorporate one or more certified components.Certified components are X-ray system components manufactured after certain dates listed in 21 CFR 1020.30(a)(i). Both diagnostic X-ray systems and computed tomography X-ray systems manufactured before November 29, 1984, are subject to the following requirements:

- The control panel containing the main power switch shall have a statement reading: **"WARNING: This X-ray unit may be dangerous to patient and operator unless safe exposure factors and operating instructions are observed."**
- Temporarily installed compatible components must bear the following labeling: "**Temporarily Installed Compatible Component.** This certified component has been assembled, installed, adjusted, and tested by me according to the instructions provided by the manufacturer. Signature; Company Name; Street Address, City, State, Zip Code, and Date of Installation."

- Temporarily installed noncompatible components must bear the following labeling: "**Temporarily Installed Noncompatible Component.** This certified component has been assembled or installed by me, but could not be assembled, installed, adjusted, and tested by me according to the instructions provided by the manufacturer because other already existing components of the system do not meet the compatibility specifications of the certified component being installed, and there are no commercially available certified components of a similar type that are compatible with the system. Signature, Company Name, Street Address, City, State, Zip Code, and Date of Installation."

Radiographic equipment (1020.31)

- If the device has the capability of overriding the positive beam limitation (PBL) in case of system failure, the override key or switch shall be labeled: "FOR X-RAY FIELD LIMITATION SYSTEM FAILURE."
- If the device has the capability of overriding the automatic X-ray field size adjustment in case of system failure, the override switch shall be labeled: "FOR X-RAY FIELD LIMITATION SYSTEM FAILURE."

Fluoroscopic equipment (1020.32)

- If the device has the capability of overriding the automatic X-ray field size adjustment in case of system failure, the override switch shall be labeled: "FOR X-RAY FIELD LIMITATION SYSTEM FAILURE."

Cabinet X-ray systems (1020.40)

- At least one indicator shall be visible from each door, access panel and port, and labeled: "X-RAY ON."
- If a cabinet X-ray system is designed to admit humans, it must bear the following additional labeling:
  - Any controls which can be used to initiate X-ray generation must be labeled:

    "CAUTION: X-RAYS PRODUCED WHEN ENERGIZED"
  - Each port shall have a clearly visible label stating:

    "CAUTION: DO NOT INSERT ANY PART OF THE BODY WHEN SYSTEM IS ENERGIZED - X-RAY HAZARD."

Light-Emitting Products

Lasers (1040.10)

Lasers are devices capable of producing intense radiation at a specific wavelength both for medical and industrial purposes. In addition to the general labeling requirements for firm name, street address, state, and zip code, lasers require labeling specific to their type, class, wavelength, and power output. Due to the numerous combinations of labeling types dictated by class, wavelength, and power output, it would not be practical to cover each in specific detail in this booklet. Instead, use the following sample label types in conjunction with the following reprints of CFR sections to demonstrate specific labeling requirements.

SAMPLE LASER LABELS

WARNING LOGOTYPE A

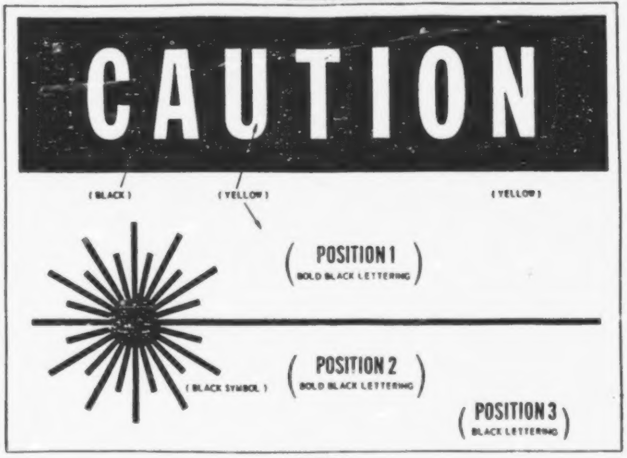
CAUTION
(BLACK)
(YELLOW)
(YELLOW)
POSITION 1
BOLD BLACK LETTERING
(BLACK SYMBOL)
POSITION 2
BOLD BLACK LETTERING
POSITION 3
BLACK LETTERING

FIGURE 1

WARNING LOGOTYPE B

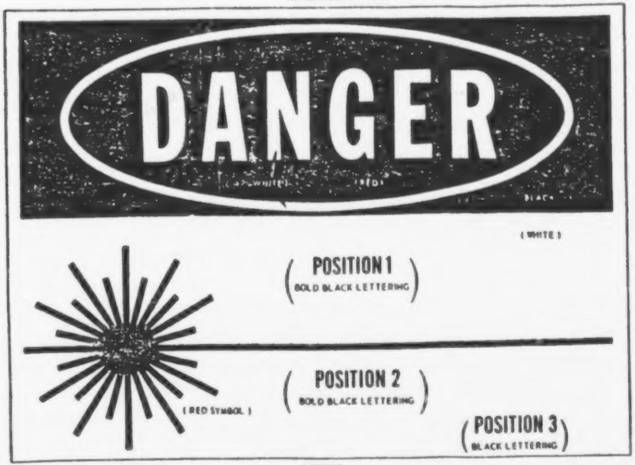
DANGER
(WHITE)
(RED)
BLACK
(WHITE)
POSITION 1
BOLD BLACK LETTERING
(RED SYMBOL)
POSITION 2
BOLD BLACK LETTERING
POSITION 3
BLACK LETTERING

FIGURE 2

REPRINT SECTIONS OF 21 CFR 1040.10(g)

(g) *Labeling requirements.* In addition to the requirements of §§ 1010.2 and 1010.3, each laser product shall be subject to the applicable labeling requirements of this paragraph.

(1) *Class IIa and II designations and warnings.* (i) Each Class IIa laser product shall have affixed a label bearing the following wording: "Class IIa Laser Product—Avoid Long-Term Viewing of Direct Laser Radiation."

(ii) Each Class II laser product shall have affixed a label bearing the warning logotype A (Figure 1 in this paragraph) and including the following wording:

[Position I on the logotype]

"LASER RADIATION—DO NOT STARE INTO BEAM"; and

[Position 3 on the logotype]

"CLASS II LASER PRODUCT".

(2) *Class IIIa and IIIb designations and warnings.* (i) Each Class IIIa laser product with an irradiance less than or equal to 2.5×10^{-3} W cm^{2-} shall have affixed a label bearing the warning logotype A (Figure 1 of paragraph (g)(1)(ii) of this section) and including the following wording:

[Position 1 on the logotype]

"LASER RADIATION—DO NOT STARE INTO BEAM OR VIEW DIRECTLY WITH OPTICAL INSTRUMENTS"; and,

[Position 3 on the logotype]

"CLASS IIIa LASER PRODUCT".

(ii) Each Class IIIa laser product with an irradiance greater than 2.5×10^{-3} W cm^{-2} shall have affixed a label bearing the warning logotype B (Figure 2 in this paragraph) and including the following wording:

[Position 1 on the logotype]

"LASER RADIATION—AVOID DIRECT EYE EXPOSURE"; and,

[Position 3 on the logotype]

"CLASS IIIa LASER PRODUCT".

(iii) Each Class IIIb laser product shall have affixed a label bearing the warning logotype B (Figure 2 of paragraph (g)(2)(ii) of this section) and including the following wording:

[Position 1 on the logotype]

"LASER RADIATION—AVOID DIRECT EXPOSURE TO BEAM"; and,

[Position 3 on the logotype]

"CLASS IIIb LASER PRODUCT".

(3) *Class IV designation and warning.* Each Class IV laser product shall have affixed a label bearing the warning logotype B (Figure 2 of paragraph (g)(2)(ii) of this section), and including the following wording:

[Position 1 on the logotype]

"LASER RADIATION—AVOID EYE OR SKIN EXPOSURE TO DIRECT OR SCATTERED RADIATION"; and,

[Position 3 on the logotype]

"CLASS IV LASER PRODUCT".

(4) *Radiation output information on warning logotype.* Each Class II, III, and IV laser product shall state in appropriate units, at position 2 on the required warning logotype, the maximum output of laser radiation, the pulse duration when appropriate, and the laser medium or emitted wavelength(s).

(5) *Aperture label.* Each laser product, except medical laser products and Class IIa laser products, shall have affixed, in close proximity to each aperture through which is emitted accessible laser or collateral radiation in excess of the accessible emission limits of Class I and Table VI of paragraph (d) of this section, a label(s) bearing the following wording as applicable.

(i) "AVOID EXPOSURE—Laser radiation is emitted from this aperture," if the radiation emitted through such aperture is laser radiation.

(ii) "AVOID EXPOSURE—Hazardous electromagnetic radiation is emitted from this aperture," if the radiation emitted through such aperture is collateral radiation described in Table VI, item 1.

(iii) "AVOID EXPOSURE—Hazardous x-rays are emitted from this aperture," if the radiation emitted through such aperture is collateral radiation described in Table VI, item 2.

(6) *Labels for noninterlocked protective housings.* For each laser product, labels shall be provided for each portion of the protective housing which has no safety interlock and which is designed to be displaced or removed during operation, maintenance, or service, and thereby could permit human access to laser or collateral radiation in excess of the limits of Class I and Table VI. Such labels shall be visible on the protective housing prior to displacement or removal of such portion of the protective housing and visible on the product in close proximity to the opening created by removal or displacement of such portion of the protective housing, and shall include the wording:

(i) "CAUTION—Laser radiation when open. DO NOT STARE INTO BEAM." for Class II accessible laser radiation.

(ii) "CAUTION—Laser radiation when open. DO NOT STARE INTO BEAM OR VIEW DIRECTLY WITH OPTICAL INSTRUMENTS." for Class IIIa accessible laser radiation with an irradiance less than or equal to 2.5×10^{-3} W cm^{-2}.

(iii) "DANGER—Laser radiation when open. AVOID DIRECT EYE EXPOSURE." for Class IIIa accessible laser radiation with an irradiance greater than 2.5×10^{-3} W cm^{-2}.

(iv) "DANGER—Laser radiation when open. AVOID DIRECT EXPOSURE TO BEAM." for Class IIIb accessible laser radiation.

(v) "DANGER—Laser radiation when open. AVOID EYE OR SKIN EXPOSURE TO DIRECT OR SCATTERED RADIATION." for Class IV accessible laser radiation.

(vi) "CAUTION—Hazardous electromagnetic radiation when open." for collateral radiation in excess of the accessible emission limits in Table VI, item 1 of paragraph (d) of this section.

(vii) "CAUTION—Hazardous x-rays when open." for collateral radiation in excess of the accessible emission limits in Table VI, item 2 of paragraph (d) of this section.

(7) *Labels for defeatably interlocked protective housings.* For each laser product, labels shall be provided for each defeatably interlocked (as described in paragraph (f)(2)(iv) of this section) portion of the protective housing which is designed to be displaced or removed during operation, maintenance, or service, and which upon interlock defeat could permit human access to laser or collateral radiation in excess of the limits of Class I or Table VI. Such labels shall be visible on the product prior to and during interlock defeat and in close proximity to the opening created by the removal or displacement of such portion of the protective housing, and shall include the wording:

(i) "CAUTION—Laser radiation when open and interlock defeated. DO NOT STARE INTO BEAM." for Class II accessible laser radiation.

(ii) "CAUTION—Laser radiation when open and interlock defeated. DO NOT STARE INTO BEAM OR VIEW DIRECTLY WITH OPTICAL INSTRUMENTS." for Class IIIa accessible laser radiation with an irradiance less than or equal to 2.5×10^{-3} W cm^{-2}.

(iii) "DANGER—Laser radiation when open and interlock defeated. AVOID DIRECT EYE EXPOSURE." for Class IIIa accessible laser radiation when an irradiance greater than 2.5×10^{-3} W cm^{-2}.

(iv) "DANGER—Laser radiation when open and interlock defeated. AVOID DIRECT EXPOSURE TO BEAM." for Class IIIb accessible laser radiation.

(v) "DANGER—Laser radiation when open and interlock defeated. AVOID EYE OR SKIN EXPOSURE TO DIRECT OR SCATTERED RADIATION." for Class IV accessible laser radiation.

(vi) "CAUTION—Hazardous electromagnetic radiation when open and interlock defeated." for collateral radiation in excess of the accessible emission limits in Table VI, item 1 of paragraph (d) of this section.

(vii) "CAUTION—Hazardous x-rays when open and interlock defeated." for collateral radiation in excess of the accesible emission limits in Table VI, item 2 of paragraph (d) of this section.

(8) *Warning for visible and/or invisible radiation.* On the labels specified in this paragraph, if the laser or collateral radiation referred to is:

(i) Invisible radiation, the word "invisible" shall appropriately precede the word "radiation"; or

(ii) Visible and invisible radiation, the words "visible and invisible" or "visible and/or invisible" shall appropriately precede the word "radiation."

(iii) Visible laser radiation only, the phrase "laser light" may replace the phrase "laser radiation."

(9) *Positioning of labels.* All labels affixed to a laser product shall be positioned so as to make unnecessary, during reading, human exposure to laser radiation in excess of the accessible emission limits of Class I radiation or the limits of collateral radiation established to Table VI of paragraph (d) of this section.

(10) *Label specifications.* Labels required by this section and § 1040.11 shall be permanently affixed to, or inscribed on, the laser product, legible, and clearly visible during operation, maintenance, or service, as appropriate. If the size, configuration, design, or function of the laser product would preclude compliance with the requirements for any required label or would render the required wording of such label inappropriate or ineffective, the Director, Office of Compliance (HFZ-300), Center for Devices and Radiological Health, on the Director's own initiative or upon written application by the manufacturer, may approve alternate means of providing such label(s) or alternate wording for such label(s) as applicable.

(h) *Informational requirements*—(1) *User information.* Manufacturers of laser products shall provide as an integral part of any user instruction or operation manual which is regularly supplied with the product, or, if not so supplied, shall cause to be provided with each laser product:

(i) Adequate instructions for assembly, operation, and maintenance, including clear warnings concerning precautions to avoid possible exposure to laser and collateral radiation in excess of the accessible emission limits in Tables I, II-A, II, III-A, III-B, and VI of paragraph (d) of this section, and a schedule of maintenance necessary to keep the product in compliance with this section and § 1040.11.

(ii) A statement of the magnitude, in appropriate units, of the pulse durations(s), maximum radiant power and, where applicable, the maximum radiant energy per pulse of the accessible laser radiation detectable in each direction in excess of the accessible emission limits in Table I of paragraph (d) of this section determined under paragraph (e) of this section.

(iii) Legible reproductions (color optional) of all labels and hazard warnings required by paragraph (g) of this section and § 1040.11 to be affixed to the laser product or provided with the laser product, including the information required for positions 1, 2, and 3 of the applicable logotype (Figure 1 of paragraph (g)(1)(ii) or Figure 2 or paragraph (g)(2)(ii) of this section). The corresponding position of each label affixed to the product shall be indicated or, if provided with the product, a statement that such labels could not be affixed to the product but were supplied with the product and a statement of the form and manner in which they were supplied shall be provided.

(iv) A listing of all controls, adjustments, and procedures for operation and maintenance, including the warning "Caution—use of controls or adjustments or performance of procedures other than those specified herein may result in hazardous radiation exposure."

(v) In the case of laser products other than laser systems, a statment of the compatibility requirements for a laser energy source that will assure compliance of the laser product with this section and § 1040.11.

(vi) In the case of laser products classified with a 7 millimeter diameter aperture stop as provided in paragraph (e)(3)(i) of this section, if the use of a 50 millimeter diameter aperture stop would result in a higher clsssification of the product, the following warning shall be included in the user information: "CAUTION—The use of optical instruments with this product will increase eye hazard."

(2) *Purchasing and servicing information.* Manufacturers of laser products shall provide or cause to be provided:

(i) In all catalogs, specification sheets, and descriptive brochures pertaining to each laser product, a legible reproduction (color optional) of the class designation and warning required by paragraph (g) of this section to be affixed to that product, including the information required for positions 1, 2, and 3 of the applicable logotype (Figure 1 of paragraph (g)(1)(ii) or Figure 2 of paragraph (g)(2)(ii) of this section).

(ii) To servicing dealers and distributors and to others upon request at a cost not to exceed the cost of preparation and distribution, adequate instructions for service adjustments and service procedures for each laser product model, including clear warnings and precautions to be taken to avoid possible exposure to laser and collateral radiation in excess of the accessible emission limits in Tables I, II-A, II, III-A, III-B, and VI of paragraph (d) of this section, and a schedule of maintenance necessary to keep the product in compliance with this section and § 1040.11; and in all such service instructions, a listing of those controls and procedures that could be utilized by persons other than the manufacturers or the manufacturer's agents to increase accessible emission levels of radiation and a clear description of the location of displaceable portions of the protective housing that could allow human access to laser or collateral radiation in excess of the accessible emission limits in Tables I, II-A, II, III-A, III-B, and VI of paragraph (d) of this section. The instructions shall include protective procedures for service personnel to avoid exposure to levels of laser and collateral radiation known to be hazardous for each procedure or sequence of procedures to be accomplished, and legible reproductions (color optional) of required labels and hazard warnings.

(i) *Modification of a certified product.* The modification of a laser product, previously certified under § 1010.2, by any person engaged in the business of manufacturing, assembling, or modifying laser products shall be construed as manufacturing under the act if the modification affects any aspect of the product's performance or intended function(s) for which this section and § 1040.11 have an applicable requirement. The manufacturer who performs such modification shall recertify and reidentify the product in accordance with the provisions of §§ 1010.2. and 1010.3.

(The information collection requirements contained in paragraph (a)(3)(ii) were approved by the Office of Management and Budget under control number 0910-0176)

[50 FR 33688, Aug. 20, 1985; 50 FR 42156, Oct. 18, 1985]

§ 1040.11 Specific purpose laser products.

(a) *Medical laser products.* Each medical laser product shall comply with all of the applicable requirements of § 1040.10 for laser products of its class. In addition, the manufacturer shall:

(1) Incorporate in each Class III or IV medical laser product a means for the measurement of the level of that laser radiation intended for irradiation of the human body. Such means may have an error in measurement of no more than 20 percent when calibrated in accordance with paragraph (a)(2) of this section. Indication of the measurement shall be in International System Units. The requirements of this paragraph do not apply to any laser radiation that is all of the following:

(i) Of a level less than the accessible limits of Class IIIa; and

(ii) Used for relative positioning of the human body; and

(iii) Not used for irradiation of the human eye for ophthalmic purposes.

(2) Supply with each Class III or IV medical laser product instructions specifying a procedure and schedule for calibration of the measurement system required by paragraph (a)(1) of this section.

(3) Affix to each medical laser product, in close proximity to each aperture through which is emitted accessible laser radiation in excess of the accessible emission limits of Class I, a label bearing the wording: "Laser aperture."

(b) *Surveying, leveling, and alignment laser products.* Each surveying, leveling, or alignment laser product shall comply with all of the applicable requirements of § 1040.10 for a Class I, IIa, II or IIIa laser product and shall not permit human access to laser radiation in excess of the accessible emission limits of Class IIIa.

(c) *Demonstration laser products.* Each demonstration laser product shall comply with all of the applicable requirements of § 1040.10 for a Class I, IIa, II, or IIIa laser product and shall not permit human access to laser radiation in excess of the accessible emission limits of Class I and, if applicable, Class IIa, Class II, or Class IIIa.

[50 FR 33702, Aug. 20, 1985]

Sunlamp products and ultraviolet lamps (1040.20)

Lamps that produce ultraviolet radiation with wavelengths in air between 200 and 400 nanometers which are designated as sunlamp products or ultraviolet lamps intended for use in sunlamp products are subject to the requirements of 1040.20.

All labels are to be affixed or inscribed on an exterior surface that can be easily seen by the person being exposed immediately before use of the product.

Sunlamp products

o Each sunlamp product shall have label(s) with the warning statement: "DANGER-Ultraviolet radiation. Avoid Overexposure. As with natural sunlight, overexposure can cause eye and skin injury and allergic reactions. Repeated exposure may cause premature aging of the skin and skin cancer. **Wear Protective Eyewear; Failure to May Result in Severe Burns or Long Term Injury to the Eyes.** Medications or cosmetics may increase your sensitivity to the ultraviolet radiation. Consult physician before using sunlamp if you are using medications or have a history of skin problems or believe yourself especially sensitive to sunlight. If you do not tan in the sun, you are unlikely to tan from use of this product."

In addition the label must also contain:

- Recommended exposure positions;
- Directions for achieving the recommended exposure positions;
- A recommended exposure schedule;
- A statement of the amount of time it may take for the expected results to appear;
- A designation of the ultraviolet lamp type to be used in the product; and
- Reproductions of the required labeling are to be prominently displayed at the beginning of the product instruction manual.

Ultraviolet lamps

o Labels for ultraviolet lamps require the following:

- The words: "Sunlamp - DANGER - Ultraviolet radiation. Follow instructions;"
- The model identification; and
- The words: "Use ONLY in fixtures equipped with a timer."

Ultrasonic Radiation-Emitting Devices

Ultrasonic therapy products (1050.10)

In addition to the general labeling requirements, ultrasonic therapy products are subject to the following additional labeling requirements:

- Operation controls--identification of operator control functions;
- Service controls--identification of the service control functions plus the statement "For service adjustment only;"
- Generators--generator labels shall state the brand name, model designation, serial number or other unique identification, ultrasonic frequency, and type of waveform;
- Applicators--applicator labels shall state the brand name, model designation, and serial number or other unique identification; the generator for which the applicator is intended; and the ultrasonic frequency, effective radiating area, maximum beam nonuniformity ratio, and type of applicator.
- Manuals--user instruction or operator manuals shall contain:
  - assembly, operation, safe use, safety procedures and precautions, and a maintenance schedule;
  - description of the special distribution of the ultrasonic radiation field and the orientation of the field with respect to the applicator;
  - description of the uncertainties in magnitude of various parameters relative to the ultrasonic energy; and
  - a listing of controls, adjustments, and procedures for operation and maintenance including a warning: "Caution: Use of controls or adjustments or performance of procedures other than those specified herein may result in hazardous exposure to ultrasonic energy."

GOVERNMENT CONTRACT DEVICE LABELING REQUIREMENTS

Introduction

Agencies of the U.S. Government such as the Department of Defense and the Veterans Administration are major purchasers, users, and warehousers of medical equipment. Large stockpiles of medical equipment are maintained in warehouses located throughout the country. In addition to working stock drawn by the military services, reserves are needed to maintain a state of war preparedness. Their varied needs and the logistics of distribution necessitate extraordinary packaging and labeling requirements. For example, supplies of hemostatic forceps must be readily available for immediate shipment, or use after prolonged storage, anywhere in the world, which includes dry desert, humid jungle environments, or sub-zero Arctic conditions. In addition, the method of transport could include dropping from an airplane, or floating the supplies to shore. FDA requirements for labeling, size, and placement are not enough; labeling must be appropriately saltwater proof and fade resistant, and may even include camouflage markings. In order to assure conformity with their needs, the U.S. Government has established military standards, or specifications, for about every imaginable piece of equipment including hardware, electronics, and medical equipment.

Labeling Specifications MIL-STD-129H

MIL-STD-129H is the most commonly used labeling standard for U.S. Government medical equipment purchases. This document is generally not a stand alone specification, but rather is used in conjunction with the device specification. For example, the military specification for a radiographic grid (known as #GG-G-00650a, Grid, Radiographic, Straight, Wafer Type) contains a heading entitled "Labeling Specifications." The labeling specifications listed call for Fed Std No. 123 (essentially a commercial package) for civilian agencies such as the General Services Administration, and requires MIL-STD-129H for the military services. When filling a Government contract these specifications take precedence over FDA requirements.

The number, size, placement, and color of the labeling would be specified in the the product specification by referring to the appropriate section of MIL-STD-129H.

The interior or unit label and exterior or shelf package label requirements contained in MIL-STD-129H are as follows:

- NSN/NATO stock number (National Serial Number)--a unique number assigned to a specific product type, regardless of manufacturer;
- Manufacturer's part number (when specifically required by the contract);
- Item description (as specified in the contract);
- Quantity and unit of issue;
- Contract, purchase, or delivery order number; and
- Level of protection and date preservation was applied.

The outer packaging requirements are:

- NSN/NATO stock number;
- Manufacturer's part number;
- Item description (as specified in the contract);
- Gross weight and volume in cubic feet;
- Level of protection and date preservation was applied;
- Proper shipping names (for hazardous items only);
- Contract, purchase order, or delivery order number; and
- Name, address, and zip code of prime contractor;
- LOGMARS*

* On 7/1/82 the Department of Defense had amended MIL-STD-129H to include a requirement for LOGMARS (Logistics Application of Automated Marking and Reading Symbology) on device labels. This labeling is the same form as the UPC (Universal Product Code) or bar code which has become an integral part of consumer items. LOGMAR labeling includes a series of digitally encoded lines containing the NSN and contract number.

DEVELOPMENT OF DEVICE LABELING

Introduction

Labeling is very important to medical device firms because there is often a direct relationship between device misuse and the labeling, especially in the directions for use. In many cases the labeling may meet the requirements of the regulations; but it may fail to fully take into consideration the user needs, possible uses other than that indicated, or other factors that may contribute to misuse of the device.

It is significant that approximately 40% of Mandatory Device Reporting (MDR) filings involve user error. FDA, the medical device industry, and the users must become more aware of this situation and work together to resolve it. One of the problem areas is labeling. In addition to the cases where there is a primary association between labeling and MDR reports, labeling can also be an "underlying" or secondary cause of misuse that leads to MDR reports.

There are three general problem areas with labeling that FDA has encountered:

Misbranding - The failure of the labeling to meet the requirements of the labeling regulations. This includes misleading statements, inadequate directions for use, or the exclusion of warning statements or contraindications;

Poor Labeling Control - This situation occurs during the manufacturing process due to a failure in the quality assurance or GMP program. Poor labeling controls result in incorrect activities such as a "mixup" in the labeling for different devices, the use of outdated labeling, or the improper application of the labeling to the device; and

Inadequate Labeling - Labeling that does not constitute misbranding but could be improved to prevent misuse or mishandling of the device.

The first two points, **misbranding,** and **poor label control** violate the letter of the law. The last, **inadequate labeling,** or **labeling that is less than it can or should be**, may not always violate the law, but can result in problems which the law was designed to prevent. Previous sections in this chapter have addressed two aspects of device labeling necessary to comply with the law. The first section in this chapter discusses the definition and causes of misbranding; the second section (Section 5) discusses areas of poor label control as addressed in the medical device GMP's. This section will address inadequate labeling and concentrate on techniques for generating and presenting text that is easy to read. It will also cover how to correlate text with figures, and how to correlate text with the device.

Labeling Problems

Two of the most important aspects to consider in labeling devices is to be cognizant of WHO will be using the device and HOW it is to be used. Once this is realized, suitable labeling can be drafted.

Often we have heard stories of parents unable to assemble "easy-to-assemble" toys on Christmas eve. Identical products with identical labeling (the instructions) may have other than the same results after assembly. Why? Because the manufacturer had failed to consider WHO. The instructions had been written at the level of someone moderately skilled in mechanics, whereas some assemblers might be confused by the operation of an electric drill. How could the problem be corrected? By the use of labeling! A simple way would be to change the labeling to read "difficult-to-assemble:" however, this might well have a negative impact on sales. The proper way, as we'll cover later, would be to draft a detailed set of instructions, using pictorials where necessary, directed at the expected experience level of the purchaser.

A manufacturer of aluminum porch awnings in Florida had been successfully marketing his product locally for over 20 years. He obtained capital and expanded his operations along the Eastern Seaboard. Soon he began to receive numerous complaints of awning collapse from the Northeast. Why? Because he failed to consider HOW. The method of attachment recommended in the instructions was insufficient to hold the added weight of predictable northeastern snowfall. In a manner similar to the above problem, the solution could be to either restrict sales to states below in the Sunbelt, or to provide an explanation and a pictorial that detailed a method of securing the awning properly to support the expected additional weight.

The same arguments hold true for medical devices whether they be catheters, heart valves, or in vitro diagnostic products. Labeling not only can be used to assure proper use of the device, but can be used to compensate for design deficiencies or alert the user to abnormal conditions.

A firm who marketed an external rigid splint began to receive reports from hospitals that patients had suffered burns and blistering on limbs where the splint had been applied. The splint consists of a coated fabric sandwiched between polymeric film and foam. In use, the foam side is placed against the limb. Water is then applied to initiate a chemical polymerization which releases heat and causes the splint to become rigid.

The label on the splint read: "**Place Opposite Side on Limb.**" In one hospital personnel stated that the label had been improperly placed on the limb side of the splint. As a result, the patients limbs were burned during the polymerization reaction. It was then discovered by the firm that some lots had the label on the wrong side of the splint, and these lots were associated with the hospitals' complaints.

In fact, this entire sequence of events probably could have been avoided by proper label content. The phrase "**Place Opposite Side on Limb**" is an ambiguous statement and does not identify any component of the splint. A more helpful descriptive statement would state:

> **"Place the (insert color, texture, etc.) Film on Outside, Away from Limb. Caution: Film Gets Hot!"**

A positive statement with the film identified by color or texture would tend to reinforce the instructions for proper placement of the label during manufacture, and placement of the splint during use on the limb.

Let's take another look at the original labeling on the splint: "Place Opposite Side on Limb." Note the geometric term, "side." In general, be very careful when using top, side, end, bottom, edge, and other geometric terms in labeling as these are often ambiguous. Always make sure the intent is obvious when the user is looking at the device.

Reducing Labeling Problems

Adequate labeling for a medical device requires proper design of labeling, controlled procurement of the labels and labeling, and proper application of labeling. Design includes labeling content that meets the requirement of the GMP regulation **as well as the needs of the user.** One should emphasize the second point: **needs of the user.** To help meet the needs of the user, there are some basic guidelines, rules, and practices that can be used to immediately improve the writing of labels and instructions.

Writers are encouraged to obtain a copy of 40,000 Words or a similarly titled book by any of the reference-book publishing companies. Most of these reference books have about four pages of punctuation rules. Using the four small pages of rules can immediately improve your writing. For example, you can avoid the common punctuation error of not using semi-colons to replace commas when needed. Also, one should obtain and use a standard college-level text on technical writing.

Further, to achieve our goals a number of concepts must be kept in mind such as: writing to the reader, referring to the actual device in labeling, obvious identification of the controls used, etc. Following is a review of these points with emphasis on how they can be used to make labeling clear and comprehensible.

Write to reader

The most serious problem is that writers tend to write to themselves. Their material is clear to them--and they mistakenly think it is as clear to others. For example, the sensitivity control on an instrument is called: "gain" control on page one of the instruction manual, "amplitude" control on page two, and "level" control in the next section. Further, the photograph in the **Introduction** shows the same control with a call-out labeled "Signal Adjust". No wonder readers are confused! Yet the author of the example knew what he was trying to write about and, most certainly, he was writing to himself.

For some devices such as home-use devices, it may be necessary to determine the reading level of the intended users.

Refer to actual device

One simple way to reduce control identity confusion as described above, reduce other types of labeling errors, and increase clarity is for authors to keep a labeled instrument, kit, or photograph(s) nearby and refer to it as they write. It is easier to write the truth when you know the truth. Make sure the terminology and descriptions in the labeling matches that on the device. Always use the same title for each given item or control throughout the manual, insert, label, or advertisement. Likewise, the same title should be used in charts, figures, or screen displays such as cathode-ray tubes, etc. Remember to:

- o write to your intended readers;
- o write with a labeled device or photographs in sight; and
- o use consistent titles.

Obvious identification of controls

Because the title of controls or other items on labels and screen displays **should be exactly the same** as in the labels on equipment, reagents, accessories, etc., authors may need to develop and use an appropriate correlation technique for corresponding titles in instruction manuals, package inserts, etc. One common technique is to use all capitals for the titles of controls in labeling. For example:

Flip the POWER switch to ON.
Press the HEAT button to switch the heater on.
In about three seconds, the READY lamp will illuminate.

With this correlation technique, the words "on" and "off" are capitalized in the labeling only when they actually appear on the instrument control panel. Note that "ON" is capitalized in "POWER switch to ON" as the actual switch has "POWER", "ON", and "OFF" printed by it. In contrast, note that "on" would not be capitalized in the example "to switch the heater on" as it is not a label of a control on the device. Also, be careful to use a simple correlation system for names of controls that is readily apparent to the intended reader.

Don't distract reader

Readers are very busy trying to learn how to use a new device. They should not be annoyed by any unnecessary distractions such as:

- o changes in format;
- o unusual typeface;
- o incorrect page numbers, and
- o incorrect figure numbers.

For a person trying to read in a hurry, a font or typestyle that the author may consider to be routine, such as script, can be a major distraction; therefore, don't use script, italics, or any other unusual or hard-to-read typefaces. Remember, you have decided to write for the benefit of the intended user. Forget about your personal preferences and use only the most common print fonts. Also, select a type size that is readable at the intended distance. For example, labeling displayed on the screen of a wall-mounted heart monitor must be readable from several feet away. Also, use a consistent format throughout the document. Also, check the format and section titles against information on the contents page. In some cases, such as for in vitro diagnostic products, the arrangement of information in the labeling may be dictated by regulation.

Page numbers should **not** be referenced in instruction or service manuals. It is very easy for the actual page numbers to be changed during the original writing or when the manual is updated. It is much better to refer to paragraph titles or paragraph numbers as they are less likely to change; and, if changed, titles are more noticeable by writers and typists than are page numbers. The use of correct figure numbers is easy--just check them.

Short and to the point

It is important to use sentence structure that will convey the intended message with a minimum of misinterpretation or need to reread. Tests have been conducted to determine the ability of readers to follow instructions in a sentence based on the number of activities to be performed. The average person's ability to follow instructions decreases rapidly when a sentence contains more than two facts. (Keep in mind your own experiences in reading instructions.) Therefore, sentences in labeling need to be short and to the point. Avoid long strings of adjectives and be specific. In many cases, a list of activities to be performed is better than burying the facts in long sentences. If it takes lots of words to get to the point, the reader will probably miss the point! Short, choppy sentences or lists are acceptable in instruction manuals and other labeling. You are not trying to entertain readers with beautiful, flowing prose--rather, you want to "shock" them into remembering key facts until they correctly perform the specified instructions. Thus:

- use short sentences;
- get to the point; and
- be specific.

Try to be as specific as possible with your instructions. For example, "ambient" or "room temperature" generally should not be used. Instead specify the desired or necessary range of operating conditions.

Gobbledygook

Another way to be more specific and shorten sentences is to avoid "gobbledygook." The following terms were collected from actual instruction manuals:

ORIGINAL	EQUIVALENT
Makes provisions for	*
Serves to	*
At the time of	When
In conjunction with	And
Carried out in	Perform
Comes up to	Reaches
Will also serve as a chance to	May
Due to the fact that	Because
Will be sure that will	Ensure
Available through the use of	*
Care should be used so as not to	Be careful
Be provided for positive determination	
Causes power to be applied to	Switches power to

In most cases, the equivalent term in the list can replace the original term. For the asterisked items, the equivalent is simply a direct statement of what is intended. Of the terms listed, the combination most often used is "makes provision for." Simply eliminating "makes provision for" and "be provided for" from labeling will result in an immediate improvement for readers.

Introduce each item

Always introduce each control, indicator, device, or subject before they are discussed in the text. The introductions should be brief and may be very brief. Keep in mind the items will be described in more detail later. Abbreviations and new or uncommon terms must be defined. The introductions and definitions prevent the reader from going into mental shock, breaking their train of thought, and asking: What is this? By then the reader has probably forgotten the last two or three facts read. Also, the reader may wonder about any "cliff-hanging" item when they resume reading. This disturbance may detract the person from fully assimilating the next instructions being read. To avoid distractions and confusion, a writer of labeling should always:

- o introduce each item; and
- o define new or uncommon terms.

With respect to definitions, a writer should never give a new meaning to an existing term. For example, quality assurance personnel of medical device firms can no longer use the word "critical" in their routine technical conversations because "critical" was given a specialized definition in the GMP regulation. To avoid this disservice, coin a special term or code number such as Class C, Code 1, or Level 2.

Accentuate key terms

Whenever it is stated in instructions that something must be done, then "must" should be underlined, set in bold type, or otherwise delineated. Likewise, caution and warning statements should be delineated by underlining, boxing, bold type, etc. Refer to any regulations or standards for a specific product and use the recommended or required caution statements. When standard terminology exists, creating new caution statements is not the best way for a writer to be creative.

Select words wisely

When large print is needed for reading at a distance or to attract attention, signs, caution labels, screen prompts, and control labels generally must be short in order to fit the available space. This situation places a burden on the writer to select terms that convey the desired message. Consider the following wording from two actual highway signs:

PLANT TRAFFIC
ENTERING HIGHWAY

NO FISHING
OFF BRIDGE

Have you ever been run over by a pachysandra? If you can't fish off the bridge, does that mean you are allowed to fish only on or from the bridge? Better choices for the intended messages are: "Traffic entering highway" or "No fishing from bridge."

Try labeling

Finally, always have someone not familiar with the product operate it **exactly** according to the draft instructions and screen displays, if any. No coaching--this is the "acid" test--good luck! During the trials, note any significant problems and make appropriate corrections to the instructions, prompts, or other labeling. You may also wish to solicit input from actual users of the product with respect to clarity, reading level, etc. The information received will reflect the problems encountered by persons trying to follow the instructions without any preconceived knowledge of the actual operation of the product.

Approval policy and procedure

Before release for use, labeling should be reviewed and approved by product development, service, marketing, quality assurance, and other appropriate managers. Manufacturers need to have a policy/procedure which covers the drafting, review, and approval of labeling. This procedure is usually used with an approval form such as the sample that follows. This form is intended for use by a medium-to-large firm; however, the checklist style can be adapted to a small firm. In the form, the areas of concern are listed under the group that is responsible for that concern. Thus, every department in the firm has input into the acceptability of the labeling.

APPROVAL FORM FOR LABELING, ADVERTISING, LITERATURE, Etc.

Return to Approval Coord. after each signature or after checking any "no" box.

Title ______________________ Document No. ___ DWG No. ____
Intended use/distribution ______________________________
Project Leader/title ________________________________
Approval Coordinator ________________________________

YES NO N/A* ENGINEERING
☐ ☐ ☐ Technical specs., installation data, & part numbers are correct.
☐ ☐ ☐ Procedural information is accurate and complete.
☐ ☐ ☐ Standards imposed by CSA, UL, IEC, etc. are met.
☐ ☐ ☐ Illustrations are technically accurate and final.
☐ ☐ ☐ Equipment protection cautions are included where necessary.
☐ ☐ ☐ Procedures have been checked on production model of the product.
☐ ☐ ☐ Changes requested in draft have been made or negotiated.
☐ ☐ ☐ Procedures are safe and effective.
☐ ☐ ☐ Final draft has been proofread.
Project Engineer: ______________ Date: ________
☐ Approved ☐ Approved with noted changes ☐ Not approved
Engineering Services Mgr: __________ Date: ________
☐ Approved ☐ Approved with noted changes ☐ Not approved

YES NO N/A SERVICE
☐ ☐ ☐ Maint./problem solving information is written for intended user.
☐ ☐ ☐ Lists part numbers needed to accomplish maintenance and repairs.
Service Manager: ______________ Date: ________
☐ Approved ☐ Approved with noted changes ☐ Not approved

YES NO N/A TRAINING AND EDUCATION
☐ ☐ ☐ Document is adequate for training purposes.
☐ ☐ ☐ Content of document agrees with experience of training specialists if experienced with this or similar product.
Training Manager: ______________ Date: ________
☐ Approved ☐ Approved with noted changes ☐ Not approved

YES NO N/A MARKETING
☐ ☐ ☐ Material is effective and complete for intended use.
☐ ☐ ☐ Material meets the needs of the international market.
☐ ☐ ☐ Material is professional and projects the company image.
☐ ☐ ☐ All claims are substantiated by data on file in the company.
Project Manager: ______________ Date: ________
☐ Approved ☐ Approved with noted changes ☐ Not approved
Director Marketing: ______________ Date: ________
☐ Approved ☐ Approved with noted changes ☐ Not approved

YES NO N/A QUALITY ASSURANCE
☐ ☐ ☐ All hazardous situations are highlighted with adequate warnings.
☐ ☐ ☐ All FDA requirements, GMP's are met.
Quality Engineer: ______________ Date: ________
☐ Approved ☐ Approved with noted changes ☐ Not approved

Drawing number __________ is entered here and at upper righthand corner by the Approval Coordinator ____________ Date: ________
N/A=not applicable signature

7 INVESTIGATIONAL DEVICE EXEMPTIONS

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INTRODUCTION

Section 520(g) of the Food. Drug. and Cosmetic Act (the Act) authorizes the Food and Drug Administration (FDA) to grant an Investigational Device Exemption (IDE) to a researcher using a device in studies undertaken to develop safety. effectiveness and other data for that device when such studies involve the use of human subjects. An approved IDE permits a device that would otherwise be subject to marketing clearance or approval to be shipped lawfully for the purpose of conducting a clinical study. An approved IDE exempts a device from certain sections of the Act. e.g.. misbranding. registration. listing. premarket notification. premarket approval. good manufacturing practices. performance standards. restricted device. banned device. and color additive requirements. There are four primary regulations regarding clinical studies included in the Code of Federal Regulations. Title 21 (21 CFR):

- o 21 CFR Part 812 provides the procedures for the conduct of clinical studies with medical devices
- o 21 CFR Part 813 provides the procedures for the conduct of clinical studies with intraocular lenses
- o 21 CFR Part 50 provides the requirements and general elements of informed consent
- o 21 CFR Part 56 provides the procedures and responsibilities for institutional review boards (IRBs)

DEFINITIONS

Persons who may become involved in research with human subjects should be familiar with the following definitions, as stated in Parts 50, 56, 812, and 813:

- Institutional review board (IRB) means any board, committee, or other group formally designated by an institution to review, to approve the initiation of, and to conduct periodic review of, biomedical research involving human subjects. The primary purpose of such review is to assure protection of the rights and welfare of human subjects. The IRB should be established, operated and should function in conformance with Part 56. The term has the same meaning as "institutional review committee" in Section 520(g) of the Act.

- Investigator means an individual who actually conducts an investigation; i.e., under whose immediate direction the investigational device is administered, dispensed to, or used on a subject. In the event of an investigation being conducted by a team of individuals, "investigator" refers to the responsible leader of that team.

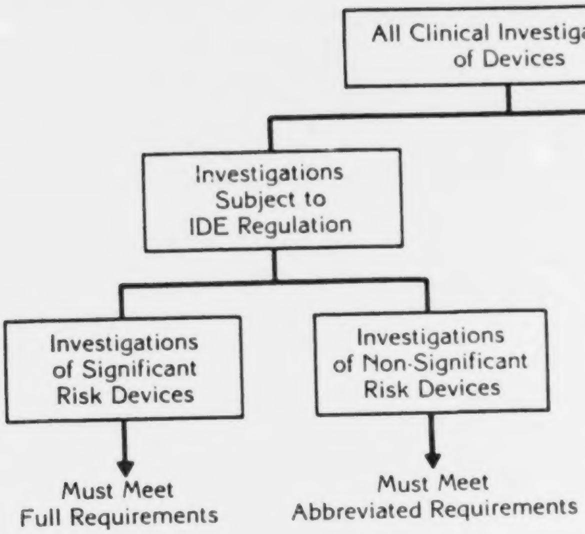
- Monitor, when used as a noun, means an individual or contract research organization designated by a sponsor to oversee the progress of an investigation. The monitor may be an employee of a sponsor, or a consultant to the sponsor, or an employee of or consultant to a contract research organization. "Monitor," when used as a verb, means to oversee an investigation.

- Sponsor means a person or other entity that initiates but does not actually conduct the investigation; yet bears the overall responsibility for the conduct of the investigation. An entity other than an individual (e.g., a corporation or an agency) which uses one or more of its own employees to conduct an investigation that it has initiated is considered to be a sponsor, not a sponsor-investigator, and the employees are considered investigators.

- Sponsor-investigator means an individual who both initiates and actually conducts, alone or with others, a clinical investigation, that is, under whose immediate direction the investigational device is administered, dispensed or used. The term does not, for example, include a corporation or agency. The obligations of a sponsor-investigator include those of an investigator and those of a sponsor.

- Implant means a device that is placed into a surgically or naturally formed cavity of the human body if the device is intended to remain there for a period of 30 days or more. In order to protect public health, FDA may determine that devices placed in subjects for shorter periods are also implants.

IDE APPLICABILITY


All Clinical Investigations of Devices
Investigations Subject to IDE Regulation
Investigations Exempt From IDE Regulation
Investigations of Significant Risk Devices
Investigations of Non-Significant Risk Devices
Must Meet Full Requirements
Must Meet Abbreviated Requirements

All device clinical investigations must have an approved IDE, or be exempt from the IDE regulation. For those device investigations which are not exempt from the IDE regulation, procedures for obtaining an approved IDE depend upon what is known about and the degree of risk presented by the device.

Investigations Exempt From the IDE Regulation

The following device investigations are exempt from the IDE regulation:

o Investigation of preamendments devices; i.e., devices in commercial distribution before the Medical Device Amendments of May 28, 1976, and substantially equivalent devices are exempt if used or investigated in accord with the labeling in effect at the time. For Class II and III devices, this exemption expires at the time premarket approval applications (PMAs) are required or an FDA mandatory standard takes effect. This exemption does **not** apply to transitional devices.*

*[Transitional devices are products previously regulated as new drugs or antibiotic drugs. These products are now subject to regulatory controls as devices under the Medical Device Amendments. The transitional provisions, which list the generic types of products involved, were published on December 16, 1977 (42 FR 63472-76). For investigational purposes, a transitional device with a notice of claimed investigational exemption for a new drug (IND) already in effect on May 28, 1976, needed an approved IDE to continue the investigation beyond January 1, 1981. Certain diagnostic transitional devices were exempt. For all other transitional devices, an approved IDE is required before clinical investigations are begun.]

- Investigation of postamendments devices, devices in commercial distribution after May 28, 1976, are exempt if the device is determined to be substantially equivalent to a preamendments device and investigated in accordance with labeling reviewed at the time equivalence was determined. For Class II and III devices, this exemption expires under the same circumstances specified for preamendments devices, above. This exemption does not apply to transitional devices.

- Diagnostic device investigations are exempt if they comply with all the applicable requirements of 809.10(c) and if the testing: (i) is noninvasive, (ii) does not require an invasive sampling procedure that presents significant risk, (iii) does not by design or intention introduce energy into a subject, and (iv) is not used as a diagnostic procedure without confirmation by another medically established diagnostic product or procedure.

- Investigations of devices undergoing consumer preference testing, testing of a modification, or testing of a combination of devices in commercial distribution are exempt if the testing is not to determine safety or effectiveness and does not put subjects at risk.

- Investigations of devices intended solely for veterinary use or for research with laboratory animals and that are so designated in the labeling are exempt.

- Investigations of custom devices, as defined in 812.3(b), are exempt unless used to determine safety or effectiveness for commercial distribution.

- Intraocular lenses (IOLs) investigations which are covered under Part 813 are exempt. All clinical investigations of IOLs are subject to FDA approval of an IDE application and must be done in accord with Part 813.

Significant vs. Nonsignificant Risk Devices

Investigations which are not exempt from the IDE regulation are subject to differing levels of control. The IDE regulation distinguishes between significant and nonsignificant risk devices. Procedures for obtaining an IDE differ accordingly.

A significant risk device is one that presents a potential for serious risk to the health, safety, or welfare of a subject and is:

- an implant; or
- used in supporting or sustaining human life; or
- substantially important in diagnosing, curing, mitigating or treating disease or in preventing impairment of human health.

Examples of significant risk devices are pacemakers, intrauterine devices (IUDs), and orthopedic implants.

A detailed discussion of significant risk is included in "Guidance on Significant and Nonsignificant Risk Device Studies" in this chapter.

Nonsignificant risk devices are those that usually do not pose a serious risk to human subjects. Examples of nonsignificant risk device investigations are daily-wear contact lenses, lens solutions, ultrasonic tooth cleaners, and foley catheters.

In deciding if a device presents significant or nonsignificant risks, the sponsor, and ultimately, the IRB should consider the device's total risks, not as compared with the risks of alternative devices or procedures. If the device is used in conjunction with a procedure involving risk, the IRB should consider the risks of the procedure in conjunction with the risks of the device. The IRB may choose to agree or disagree with the sponsor's initial determination of degree of risk. Sponsors must notify FDA when an IRB determines that a device, judged by the sponsor not to present a significant risk, is, in fact, a significant risk device. FDA may come to a different conclusion than that reached by the sponsor and the IRB, and FDA may overrule a decision.

REQUIREMENTS FOR THE INVESTIGATION OF NONSIGNIFICANT RISK DEVICES

The determination that a device presents nonsignificant or significant risk is initially made by the sponsor. The proposed study is then submitted to an IRB for review. IRBs may ask for and obtain certain information prior to determining the risk status of the device. A risk assessment determination and the rationale of the sponsor's decision must be provided to the IRB by the sponsor.

Sponsors of studies involving nonsignificant risk devices do not need to submit IDE applications to FDA, unless FDA notifies them that submission of an IDE application is required. FDA considers a nonsignificant risk device investigation to have an approved IDE application if the sponsor obtains a nonsignificant risk determination from the IRB, after presenting the IRB with a brief explanation of why the device does not pose a significant risk, and obtains IRB approval for the study.

If any of the reviewing IRBs disagree with the sponsor's assessment of nonsignificant risk and believe that an investigational device poses a significant risk, sponsors are required to notify FDA, in which case submission of an IDE application to FDA may be required.

In order for a sponsor to be considered to have an approved IDE for a nonsignificant risk device, the sponsor must:

- label the device in accordance with the IDE regulation (812.5);
- maintain IRB approval throughout the investigation;
- ensure that investigators obtain and document informed consent under Part 50 for each subject under their care, unless documentation is waived by an IRB in accordance with 56.109(c);
- comply with IDE requirements, as specified in 812, for monitoring the investigation, maintaining records, and making reports;
- ensure that participating investigators maintain records and make reports as required;
- comply with prohibitions on promotion, test marketing, commercialization of investigational devices, and unduly prolonging an investigation.

REQUIREMENTS FOR THE INVESTIGATION OF SIGNIFICANT RISK DEVICES

A sponsor of a significant risk device investigation must obtain approval from both FDA and an IRB before beginning an investigation. Under the requirements of the IDE regulation, sponsors must have an approved IDE application in order to conduct clinical investigations on the safety and effectiveness of significant risk devices. To obtain IDE approval for a significant risk device investigation, a sponsor must:

- develop an investigational plan and assemble reports of prior investigations;
- select qualified investigators, provide them with all necessary information on the plan and on reports of prior investigation, and obtain signed agreements from them;
- submit the investigational plan and reports of prior investigations to the IRB for review and approval; and
- submit a complete IDE application to FDA for review and obtain FDA approval of the IDE.

An IDE application is considered approved 30 days after a complete IDE application has been received by FDA, unless FDA otherwise informs the sponsor. The sponsor may submit an IDE application before, concurrently with, or after IRB review.

THE CONTENT OF AN IDE APPLICATION

Original Applications

There is no preprinted form for IDE applications. However, 812.20(b) details the kinds of information that must be included in an IDE application. This information includes:

1. Name and address of sponsor.

2. Complete reports of prior investigation (812.27) including:

    - results of all prior clinical, animal, and laboratory testing;
    - bibliography of relevant publications, whether adverse or supportive; and
    - summary of relevant unpublished information, whether adverse or supportive;
    - statement of extent of compliance with the Good Laboratory Practices regulation.

3. Complete investigational plan (812.25) or a comprehensive summary in the following order:

    - name and intended use of the device and objectives and duration of the investigation;
    - written protocol describing the methodology and an analysis of the protocol demonstrating the scientific soundness of the investigation;
    - risk analysis [812.25(c)];
    - description of the device, important components, and principles of operation and anticipated changes in the device during the study; and
    - written monitoring procedures and names and addresses of monitors.

4. Description of methods, facilities, and controls used for manufacture, processing, packing, storage, and installation of the device.

5. Example of the agreement to be signed by investigators and a list of investigator names and addresses.

6. Certification that all investigators have signed the agreement and that new investigators will sign the agreement.

7. List of names, addresses, and chairpersons of each IRB that has or will be asked to review the investigation and certification of IRB action concerning the investigation (when available).

8. Name and address of any institution (other than those above) where a part of the investigation may be conducted.

9. The amount, if any, charged for the device and an explanation of why sale does not constitute commercialization.

10. A claim for categorical exclusion or an environmental assessment under Part 25 - Environmental Impact Consideration regulation.

11. All labeling for the device.

12. Copies of all informed consent forms and all related information materials to be provided to subjects that meet the requirements of Part 50.

13. Any other relevant information that FDA requests for review of the IDE application.

Information previously submitted to FDA may be referenced, if authorized.

FDA offers the following suggestions on preparing and submitting IDE applications. Sponsors filing applications should do the following:

- Submit all items in triplicate. If an amendment or supplement refers to more than one IDE, three copies of the submission must be submitted for every IDE referenced.
- Use 3-hole punched paper.
- The left margin should be at least 1 1/2" wide to allow binding into jackets.
- If submissions exceed 2" in thickness, separate into volumes and identify volume number.
- Clearly and prominently identify amendments and supplements by IDE number and the type of submission (e.g., G860000; Supplement; Addition of New Institution).

Supplemental Applications

Supplemental applications are required for:

- Changes in the investigational plan that may affect the scientific soundness of the investigation or the rights, safety or welfare of the subjects. In this case, the sponsor is required to (1) submit the supplemental application to FDA, and (2) obtain FDA approval for any such change and, when the change involves the rights, safety or welfare of subjects, obtain IRB approval before implementation.

- o Addition of new institutions or facilities. In this case, the sponsor is required to submit (1) certification of IRB approval, (2) information updating the IDE application, if the investigation is changed, and (3) a description of any modifications required by the IRB as conditions of approval.

Note that while submission of IRB approval is necessary, it is not a precondition for FDA's review of such a request.

Unless FDA specifically grants a waiver from these requirements, the sponsor may not begin the investigation at a new institution until:

- o IRB approval is obtained;
- o FDA receives certification of IRB approval; and
- o FDA approves the supplemental application.

Prior FDA approval is not required, for changes or deviations in the investigational plan to protect the life or physical well-being of a subject in an emergency. However, the sponsor must report such changes to FDA within 5 working days.

FDA Review

FDA reviews each IDE application. Sponsors are notified in writing of the date FDA receives their original application and the number assigned. Receipt of supplements and amendments are not acknowledged. Within 30 days from the date of receipt FDA will approve as submitted, approve with conditions, or disapprove an IDE application. In cases of disapproval, a sponsor has the opportunity to respond to the deficiencies or request a hearing under Part 16.

Investigations may begin after IRB approval has been obtained and at the expiration of 30 days after FDA receives the application, unless FDA notifies the sponsor that it may not begin. FDA prepares a written response to such original IDE application and these letters are issued approximately 28 days after the date of receipt. While FDA may contact the sponsor by telephone to notify them of disapproval decision, the sponsor should contact FDA by the 30th day to verify the status of FDA's decision prior to proceeding with the investigation.

Sponsors who wish to conduct investigations of banned devices shall not begin an investigation before obtaining written FDA approval. All investigations of banned devices are considered to present significant risk.

RESPONSIBILITIES OF PARTICIPANTS

The IDE regulation specifies basic requirements for conducting investigations and identifies the responsibilities of participants. Sponsors are required to:

- o submit an IDE application and supplemental applications to FDA;

- o ensure that both FDA and an IRB have approved the application (or supplemental application) before beginning an investigation (or part of an investigation);

- select investigators qualified by training and experience to investigate the device and obtain signed investigator agreements as well as curricula vitae;
- ensure proper monitoring of the investigation directly or through qualified monitors, including immediate evaluation of unanticipated adverse device effects and termination of investigations that present unreasonable risk to the subject;
- provide investigators with copies of the investigational plan and reports of prior investigations;
- secure compliance or discontinue shipment of device if an investigator is not complying with the signed agreement, investigation plan, or stipulation of approval by FDA or an IRB;
- ship the devices only to qualified investigators;
- ensure that IRBs and FDA are informed of significant new information about the investigation;
- secure IRB and FDA approval for resumption of terminated investigations;
- maintain accurate, complete and current records on the investigation, including correspondence, records of shipment or disposition, signed investigator agreements, and records of adverse effects;
- prepare and submit complete, accurate and timely reports, including reports of unanticipated adverse device effects, withdrawal of IRB approval, withdrawal of FDA approval (to be submitted to IRBs and investigators), investigator lists, recall and device dispositions, emergency protocol deviations, device use without informed consent, and annual progress reports and a final report;
- avoid commercialization or test marketing of the device under investigation;
- avoid representing the investigational device to be safe and effective for its investigated use;
- ensure that the investigation is not unduly prolonged; and
- permit FDA inspection.

Institutional Review Board

IRBs must comply with all applicable requirements of the IRB regulation (Part 56) in the review of clinical investigation involving human subjects and Informed Consent (Part 50) and the IDE regulations (Part 812) in reviewing and approving device investigations.

IRBs must:

- be composed of qualified members as specified in the IRB regulation;
- adopt and follow written review procedures;

- ensure that IRB business is conducted with a majority of members present and that members with conflicts of interest do not participate in the review of investigations;

- review all research activities;

- evaluate risks and benefits to subjects, knowledge to be gained, and the adequacy of informed consent;

- review proposed investigations in a timely manner;

- notify investigators, officials of the institutions and sponsors, if appropriate, of IRB decisions and the basis for them;

- maintain certain records in accordance with Part 56; and

- permit authorized FDA employees to inspect records.

Investigators must:

- obtain IRB and FDA approval before allowing a subject to participate in the investigation;

- conduct investigations according to signed agreements, the investigational plan, applicable FDA regulations, and any other conditions of approval imposed by an IRB or FDA;

- ensure informed consent is properly obtained and documented in accordance with Part 50;

- supervise the use of devices on those subjects who are in the investigator's area of supervision;

- maintain records relating to investigations, including correspondence, shipment records, subjects' case histories and exposure to the device, informed consent, adverse device effects, and protocol deviations;

- prepare and submit reports including unanticipated device adverse effects, withdrawal of IRB approval, progress and final reports, deviations from investigational plan and device use without informed consent; and

- permit FDA inspection.

A summary of the responsibilities for participants are included in Tables I, II, and III that follow.

INSPECTIONAL AUTHORITY

- FDA has authority to inspect facilities at which investigational devices are manufactured, processed, held or used; and

- Sponsors, IRBs and investigators are required to permit authorized FDA employees reasonable access at reasonable times to inspect and copy records on an investigation.

Table I
Responsibilities for Maintaining Records

	Records	Maintained by	
		Investigator	Sponsor
SIGNIFICANT RISK DEVICE	- - All Correspondence Pertaining to the Investigation	✓	✓
	- - Shipment, Receipt, Disposition	✓	✓
	- - Device Administration and Use	✓	—
	- - Subject Case Histories	✓	—
	- - Informed Consent	✓	—
	- - Protocols and Reason for Deviations from Protocol	✓	—
	- - Adverse Device Effects and Complaints	✓	✓
	- - Signed Investigator Agreements	—	✓
	- - Membership/Employment/Conflicts of Interest	—	—
	- - Minutes of Meetings	—	—
NONSIGNIFICANT RISK DEVICE	- - Name and Intended Use of Device	—	✓
	- - Brief Explanation of Why Device Does Not Involve Significant Risk	—	✓
	- - Name and Addresses of Investigator(s) and IRBs	—	✓
	- - Degree GMPs Followed	—	✓
	- - Informed Consent	✓	—
	- - Adverse Device Effects and Complaints	—	✓

Records
Maintained by IRB

- - Research Proposals Reviewed
- - Sample Consent Documents
- - Investigator Progress Reports
- - Reports of Subject Injuries
- - Meeting Minutes
    Attendance
    Actions Taken
    Votes
    Basis for Changes or Disapproval
    Summary of Controverted Issues
- - Records of Continuing Reviews
- - Correspondence
- - Membership
- - Written Procedures
- - Statements of Significant New Findings
- - Record Retention

Table II
Responsibilities For Preparing and Submitting Reports For Nonsignificant Risk Devices

TYPE OF REPORT	REPORT PREPARED BY	
	INVESTIGATORS FOR	SPONSORS FOR
Unanticipated Adverse Effect Evaluation	Sponsors and IRBs	FDA, investigators and IRBs
Withdrawal of IRB Approval	Sponsors	FDA, Investigators and IRBs
Progress Report	N/A	IRBs
Final Report	N/A	IRBs
Inability to Obtain Informed Consent	Sponsors and IRBs	FDA
Withdrawal of FDA Approval	N/A	IRBs and Investigators
Recall and Device Disposition	N/A	FDA and IRBs
Significant Risk Determinations	N/A	FDA

Table III
Responsibilities For Preparing and Submitting Reports For Significant Risk Devices

TYPE OF REPORT	REPORT PREPARED BY	
	INVESTIGATORS FOR	SPONSORS FOR
Unanticipated Adverse Effect Evaluation	Sponsors and IRBs	FDA, Investigators and IRBs
Withdrawal of IRB Approval	Sponsors	FDA, Investigators and IRBs
Progress Report	Sponsors, Monitors and IRBs	FDA and IRBs
Final Report	Sponsors and IRBs	FDA, Investigators and IRBs
Emergencies (Protocol Deviations)	Sponsors and IRBs	FDA
Inability to Obtain Informed Consent	Sponsors and IRBs	FDA
Withdrawal of FDA Approval	N/A	IRBs and Investigators
Current Investigator List	N/A	FDA
Recall and Device Disposition	N/A	FDA and IRBs
Records Maintenance Transfer	FDA	FDA
Significant Risk Determinations	N/A	FDA

ADDITIONAL GUIDANCE

Guidance is available to interested persons and sponsors who are unsure of whether an IDE application may be required or who may need other information and literature.

For assistance, contact:

IDE Staff, HFZ-403
Center for Devices and Radiological Health
Food and Drug Administration
5600 Fishers Lane
Rockville, Maryland 20857
(301) 427-8162

or

Division of Small Manufacturers Assistance
Food and Drug Administration
5600 Fishers Lane
Rockville, Maryland 20857
(301) 443-6597
800-638-2041 (toll free)

For assistance on responsibilities of IRBs, contact:

Office of Associate Commissioner for Health Affairs, HFY-20
Food and Drug Administration
5600 Fishers Lane
Rockville, Maryland 20857
(301) 443-1382

INVESTIGATIONAL DEVICE EXEMPTION REGULATION QUESTIONS AND ANSWERS

Part 812: Investigational Device Exemption Regulation

Subpart A: General Provisions

Scope (812.1)

Q. If the sponsor of a device investigation has an approved IDE. is the manufacturer of the device subject to the device GMP regulation?

A. No. A sponsor of an IDE approved investigation is not subject to GMPs. However. an IDE application must describe the methods. facilities. and controls used for the manufacture. processing. packing. storage. and. if appropriate. installation of the device. If the sponsor intends to comply with the GMP regulation. the IDE application should state so. The sponsor of a nonsignificant risk device investigation who intends to comply with the GMP regulation should keep on file a statement of the extent to which they will follow this regulation. Investigations of devices which are exempt from the IDE regulation should comply with GMPs.

Q. Are devices with an approved IDE exempt from Section 501 on adulteration or Section 518 of the Act on notification and other remedies?

A. No. An investigational device may be considered adulterated under Section 501 of the Act if the sponsor or investigator fails to comply with a requirement of the IDE regulation (Part 812). Section 518 is applicable. however. only to devices in commercial distribution. and since investigational devices are not to be commercialized. Section 518 is not relevant to devices with an approved IDE.

Applicability (812.2)

Q. When is an IDE application required for a nonsignificant risk device?

A. Following the IRB approval of a nonsignificant risk device investigation. the investigation is deemed to have an approved IDE. and an application to FDA is not necessary.

The IDE regulation allows FDA to require that an application be submitted for a nonsignificant risk device; nevertheless. FDA anticipates that such a requirement will be rare. This may occur (1) if reports of unanticipated adverse reactions suggest that the device presents a significant risk; (2) if FDA inspections indicate that a sponsor's risk assessment is in error; (3) if an IRB determines that a device is a significant risk device; or (4) if there is any other important reason for FDA oversight of the investigation.

Q. If a device has several uses. one of which involves significant risk. are investigations of the nonsignificant risk uses subject to the significant risk requirements of the IDE regulation?

A. No. If a device is being tested for a use that does not present significant risk. it is subject only to those sections of the IDE regulation applicable to nonsignificant risk devices. If that same device is used in an investigation that presents significant risk. it is subject to the full IDE requirements for that use.

Q. The IDE regulation states that sponsors are required to maintain IRB approval. What does this mean?

A. This means the sponsor must ensure that the investigation constantly meets IRB requirements. An IRB must review clinical investigations at least once each year.

Q. Must sponsors of nonsignificant risk device investigations submit investigational plans and reports of previous investigations to IRBs to obtain their approval?

A. The IDE regulations do not state which materials must go to IRBs. However, the "Guidance on Significant and Nonsignificant Risk Devices" included in this chapter addresses what should be submitted to IRBs. In addition, the IRB regulation does specify the criteria and procedures by which an IRB may approve FDA regulated research. In particular, 56.111(a) requires an IRB, before approving research, to determine that the following requirements are satisfied:

- o risks to subjects are minimized;
- o risks to subjects are reasonable in relation to the anticipated benefits and the knowledge to be gained;
- o selection of subjects is equitable; and
- o informed consent is obtained and documented in accordance with Part 50.

Where appropriate, the research plan must make adequate provision for monitoring the data collected to ensure subject safety, protect subject privacy, maintain data confidentiality, and protect vulnerable subject populations.

The IRB regulation allows IRBs to determine what information is needed to satisfy these requirements, and FDA encourages reasonable, independent decision making among IRBs. For certain investigations, an IRB may desire minimal information upon which to base a decision. For other investigations, an IRB may need as much information as normally appears in an IDE application to FDA, even though the IRB may subsequently determine, in light of this information, that the investigational device does not present a significant risk. For example, an IRB might ask the sponsor whether other IRBs have reviewed the proposed study, and what determination was made.

Q. Are devices in commercial distribution before the May 28, 1976, enactment date of the Amendments, exempt from IDE requirements?

A. In general, yes. The IDE regulation exempts preamendments devices, other then "transitional" devices, if they are used or investigated in accordance with labeling in effect before May 28, 1976. For Class II devices, this exemption expires on the effective data of a regulatory performance standard. If the devices do not meet the performance standard, they may be distributed only under an approved IDE. For Class III preamendments devices, this exemption expires 90 days after the effective date of the FDA regulation or order calling for a PMA submission, or on a later date specified by FDA.

Q. Are all devices marketed after May 28, 1976, subject to the IDE regulation?

A. Except for "transitional" devices, the IDE regulation exempts postamendment devices that FDA has determined to be substantially equivalent to preamendment devices if they are used according to the labeling that FDA reviewed when determining substantial equivalence. This exemption does not apply to a Class II device after a performance standard is established for the device under Section 514 or to a Class III device after an order calling for the submission of a PMA is issued under Section 515(b) of the Act.

Q. Must a determination of substantial equivalence to a preamendment device be sought from FDA before initiating a clinical investigation?

A. No, but FDA encourages sponsors to consider whether the device may be substantially equivalent and pursue this opportunity if appropriate. A determination from FDA may prevent a sponsor from spending money and effort for substantially equivalent devices. In order to substantiate a claim of equivalence, FDA may require clinical data which must be obtained in accordance with the IDE regulation. Certain device features that FDA considers in determining substantial equivalence are listed in 807.87.

Q. Are exempt investigations subject to the requirements of the IRB and informed consent regulations?

A. Yes. Exempt investigations that may be used to support research or marketing applications and which involve human subjects are subject to the requirements of the IRB (Part 56) and informed consent (Part 50) regulations.

Q. What is the difference between "testing which is noninvasive" and "testing which does not require an invasive sampling procedure that presents significant risk?"

A. "Testing which is noninvasive" focuses on the device and means that the device is "noninvasive" as defined in the IDE regulation. For example, a stethoscope would be a device for which testing is noninvasive. A laparoscope involves invasive testing.

The phrase "testing which does not require an invasive sampling procedure that presents significant risk" focuses not on the device, but rather on how the sample to be analyzed with an in vitro diagnostic device is obtained. For example, obtaining a throat culture for microbiological testing or venipuncture would be an invasive sampling procedure that does not present significant risk. A spinal tap would, on the other hand, present significant risk.

Q. If a diagnostic device investigation is exempt from the IDE regulations, must the sponsor comply with any other requirements?

A. The sponsor must meet all applicable requirements of the FD&C Act. The sponsor must comply with the in vitro diagnostic product labeling requirements, the informed consent and IRB approval requirements, and any applicable radiological health requirements. The device investigation will remain exempt, however, only if the sponsor ensures that the device results are confirmed with a medically established diagnostic device or procedure. A sponsor who wishes to export an investigational device must meet the export requirements for investigational devices.

Q. Is a device that introduces energy into a subject's body a significant risk device?

A. Such a device may be a significant risk device depending upon the potential for harm to the subject caused by the energy introduction.

Q. If a radiation-emitting investigational device is subject to the IDE regulation, is it also subject to the CDRH regulations on radiation-emitting products?

A. An IDE grants exemption from certain provisions of the Act; it does not grant exemption from other Federal, State, or local regulations. Certain radiation-emitting electronic products may be investigational medical devices and are subject to radiological health regulations enforced by CDRH; e.g., product performance standards for products such as lasers and diagnostic X-rays. Under these regulations, however, some variances may be granted. Such variances must be applied for separately. FDA will make every effort to coordinate the process to avoid duplicative paperwork; e.g., one submission may reference another.

Q. What is meant by the phrase "testing of a modification?"

A. This refers to testing a change in a commercially available device. For example, anesthesiologists may alter commercially available anesthesiology devices to suit particular hospital or patient conditions. A smaller breathing circuit may be substituted for pediatric use or the tubing lengthened or shortened, depending on the configuration of the operating room. To be exempted from the IDE regulation, however, this testing must not be for the purpose of determining safety and effectiveness and must not put subjects at risk.

Q. Are custom devices exempt from the IDE regulation?

A. Yes, if the devices are not being tested to determine safety or effectiveness for purposes of commercial distribution. Custom devices are still subject to all provisions of the Act except Sections 510(k), Premarket Notification; 514, Performance Standards; and 515, Premarket Approval.

Q. Does the IDE regulation apply to the components of significant and nonsignificant risk devices?

A. Yes. The regulation applies to a "device" as defined in the Act. Any components, accessories, and parts used with the device and not used as separate and independent devices are subject to the regulation. The investigational plan must include a description of important device components.

Q. Are acupuncture devices investigational devices?

A. Yes. This was announced in the Federal Register notices of March 9, 1973, and November 2, 1979.

Investigations Subject to Notices of Claimed Investigational Exemption for a New Drug (INDs) (812.2(e))

Q. Are transitional devices exempt from the IDE regulation?

A. Only certain diagnostic transitional devices are exempt (e.g., carcinoembryonic antigen (CEA)), provided that the exemption criteria in 812.2(c)(3) are met. No transitional devices other than diagnostic devices that meet the criteria in 812.2(c)(3) are exempt. (For a definition of "transitional device," see the last question and answer under the next section, "Definition" (812.3.))

Q. Can a transitional device be either a significant risk device or a nonsignificant risk device?

A. Yes.

Q. How are the transitional devices affected by the IDE regulation?

A. New investigations of transitional devices are subject to the IDE regulation. Transitional device investigations begun prior to July 16, 1980, however, were required to have approved IND applications. These investigations were subject to INDs until 90 days after the effective date of the IDE regulation. FDA extended this deadline until January 19, 1981. To continue an investigation after that date, there must be an approved IDE.

Clinical investigations completed before January 19, 1981, however, did not require an IDE. In order for an IND significant risk device investigation to be approved as an IDE, the sponsor would have had to obtain IRB approval after presenting the IRB with the investigational plan and a report of prior investigation. The sponsor was required to certify IRB approval, and any expansion of the existing protocol required a supplemental IDE application.

If an IND clinical investigation continuing beyond January 19, 1981, does not involve a significant risk device, the limited records and reports requirements for clinical investigations of nonsignificant risk devices must be followed.

Definitions (812.3)

Q. Is it possible for a device implanted for less than 30 days to be a significant risk device?

A. Yes. FDA may declare such a device to be a significant risk device, but the determination would be made on a case-by-case basis. For example, the determination that a diaphragm is a significant risk device is based on the intended use of the device rather than on its nature as an implant.

Q. What is meant by the term "investigational testing?"

A. This is testing to determine the safety or efficacy of a device and may involve either preclinical or clinical investigations. The IDE regulation applies only to clinical investigations of devices. Nevertheless, the regulation does contain labeling requirements for investigational devices shipped for animal research.

Q. May a consumer preference test involve human subjects?

A. No. This testing involves humans, but not as subjects. The regulation defines a subject as a participant in the testing of an investigational device to determine if it is safe and effective. Consumer preference testing must not expose humans to risk.

Q. What are transitional devices?

A. Transitional devices are products previously regulated as new drugs or antibiotic drugs that are now subject to regulatory controls as devices under the Medical Device Amendments. The official notice on transitional devices appeared in the Federal Register of December 16, 1977. That notice discusses transitional devices in greater detail and includes the list of the categories of transitional devices. Soft contact lenses, tissue adhesives, and surgical sutures are examples of transitional devices.

Labeling of Investigational Devices (812.5)

Q. How should investigational devices covered by an approved IDE be labeled?

A. The labeling must contain the name and place of business of the manufacturer, packer, or distributor; the quantity of contents; all relevant contraindications, hazards, adverse effects, interfering substances or devices, warnings, and precautions; and the statement: "Caution - Investigational Device. Limited by Federal (or United States) Law to Investigational Use."

Q. How should an investigational device be labeled when it is shipped from a sponsor's plant to another sponsor facility for repacking?

A. In this instance the investigational device should be labeled: "Caution: For Manufacturing, Processing, or Repacking." When the device leaves the repacker, it should carry the information specified in the previous answer.

Q. What are the labeling requirements for investigational in vitro diagnostic devices?

A. The labeling of an investigational in vitro diagnostic device that is exempt from the requirements of the IDE regulation must comply with 809.10(c). All other investigational in vitro diagnostic devices, significant or nonsignificant risk, must comply with the applicable requirements of the IDE regulation and must be labeled in accordance with 812.5.

Q. May investigational device labeling contain safety or effectiveness claims?

A. No. The labeling may not represent the device to be safe or effective for the purpose for which it is being investigated.

Prohibition of Promotion and Other Practices (812.7)

Q. Does the prohibition on commercialization authorize FDA to audit a sponsor's financial records?

A. Yes. If an audit is necessary for FDA to determine whether a sponsor's charge for a device exceeds the costs of manufacturing, research, development, and handling, FDA may demand proof that no profit has been earned. A sponsor may have to submit certain financial records to demonstrate that the prohibition against commercialization has not been violated.

Q. Does the prohibition against promotion of an investigational device apply to investigators as well?

A. Yes. Investigators must not represent to potential subjects that investigational devices are safe and effective for the purposes for which they are being investigated. Investigators may publish the results of investigations in scientific journals and may express their views based upon their experience with devices. Reprints of such articles, however, cannot be used to promote investigational devices.

Q. May a device investigation conducted under an approved IDE application be continued after a PMA has been submitted?

A. Yes, if the investigation remains within the framework of the approved IDE. If the PMA is not approved because the data presented is not sufficient to establish safety and efficacy, the investigation may be continued provided the testing is still within the framework of the IDE protocol. If FDA determines that premarket approval cannot be justified, the investigation should be promptly terminated. If a PMA is approved, there may no longer be a need for the IDE. FDA may occasionally require postapproval studies of the device for its intended use, e.g., long-term toxicity studies. These types of postapproval studies need not be conducted under an IDE since the device is being used within the approved indications of use.

Import and Export Requirements (812.18)

Q. Are all investigational devices subject to FDA export approval?

A. Yes.

Q. How does a sponsor obtain FDA export approval?

A. The sponsor must write FDA's Office of Compliance, HFZ-323, requesting permission and stating that the device: (1) meets the foreign purchaser's specifications; (2) is not in conflict with the laws of the country to which it is intended for export; (3) is shipped with labeling on the outside of the package that states the device is intended for export; and (4) is not sold or offered for sale in domestic commerce unless FDA authorizes sale of the device. The sponsor must provide documentation, in English, from the appropriate agency or individual in the foreign country that the country approves the device for import. FDA reviews these requests and responds to a sponsor in writing.

Subpart B: Application and Administrative Actions

Application (812.20)

Q. If FDA requests additional information concerning an investigation, what options does the sponsor have in responding?

A. The sponsor may decide whether to give the information to FDA. If the choice is made not to give FDA this information, and the IDE is not yet approved, the sponsor may treat FDA's request as a disapproval of an IDE application and may ask for a hearing under Part 16. If the study is ongoing and the sponsor refuses to produce the information, FDA may consider withdrawing approval of the application. This is also subject to a hearing.

Investigational Plan (812.25)

Q. Must a sponsor supply FDA with each of the various types of informed consent forms from different institutions to be used in a significant risk device investigation?

A. No. FDA permits the sponsor to submit their consent form, knowing that each participating institution may modify it for their needs, provided that the required elements presented in the sponsor's consent are basically the same in each institution's consent form.

Q. What is meant by the phrase "sponsor certification of IRB action?"

A. This means a sponsor's statement of an IRB's action on an investigation; e.g., disagreement with the sponsor's risk assessment, approval, denial, or approval with conditions.

Report of Prior Investigations (812.27)

Q. Is previous animal testing required in all instances?

A. No, not for all devices. If animal testing is relevant, it should all be completed before an IDE application is submitted. FDA will not approve the application until such testing is completed. Generally, animal testing must be conducted in compliance with the Good Laboratory Practice regulation (Part 58).

Supplemental Applications (812.35)

Q. Must a sponsor notify FDA of all changes made in a significant risk device investigation?

A. Sponsors of significant risk devices must submit a supplemental application for: (1) changes in the investigational plan that may affect its scientific soundness or the rights, safety or welfare of the subjects, and (2) the addition of new institutions or facilities.

Before implementation of changes in the investigational plan, the sponsor must obtain FDA approval for any such change and IRB approval when the change involves the rights, safety or welfare of subjects.

A sponsor may not initiate the investigation at a new institution until both FDA and IRB approval is obtained and FDA receives certification of IRB approval. On a case-by-case basis. FDA may waive some requirements for adding new institutions by permitting institutions to begin a study prior to FDA's receipt of certification of IRB approval.

Q. Is prior approval required for changes in the investigational plan in the case of an emergency?

A. Changes or deviations from the investigational plan to protect the life or physical well-being of a subject in an emergency do not require prior FDA approval. However. the investigator must notify the sponsor and the reviewing IRB within 5 working days of the emergency use and the sponsor must notify FDA within 5 working days after learning of it.

Q. What is the time limit for FDA review of supplemental applications?

A. Within 30 days after receiving the application. FDA notifies the sponsor of its decision. i.e.. approval. disapproval. approval with modifications. or request for additional information.

Confidentially of data and information (812.38)

Q. Will FDA release information in a pending or approved IDE under the FOI Act or under Section 520(h) of the FD&C Act?

A. No IDE data are released until: (1) FDA determines that the information had been previously disclosed to the public: (2) FDA approves a PMA for a device subject to an IDE: or (3) the device has in effect a PDP notice of completion. There are exceptions to this general rule. such as when FDA determines that it is in the public interest to release a summary of selected portions of the safety and effectiveness data. a subject in the investigation requests information on adverse effects pertinent to his or her use. or FDA. on its own initiative. discloses this information to a subject. FDA discloses data and information in an IDE file in accordance with FDA Freedom of Information regulations. Upon request. FDA will release a summary of safety and effectiveness information on a banned device IDE application that FDA has approved or disapproved. or for which FDA has withdrawn approval. Trade secret and confidential commercial information will not be disclosed from an IDE.

Subpart C: Responsibilities of Sponsors

General responsibilities of sponsors (812.40)

Q. Must all investigations have sponsors? Who can serve as the sponsor of an investigation?

A. All investigations must have sponsors. A sponsor may be any person or group (e.g.. manufacturer. educational institution. hospital. or Government agency) that initiates a clinical investigation and is willing to accept a sponsor's responsibilities. An investigator may also be a sponsor-investigator. The sponsor must be a resident of the U.S.

Selecting investigators and monitors (812.43)

Q. Who is responsible for the selection of investigators? What criteria should be used in the selection process?

A. Sponsors are responsible for selecting investigators and should establish selection criteria based on the training and experience required to investigate the safety and effectiveness of devices. On occasion FDA will provide minimum criteria.

Q. May a health professional, such as a nurse or therapist, be qualified as an investigator? May a nurse or other health professional use the device under supervision of an investigator?

A. Yes. A nurse, therapist, etc., may be an investigator if the individual's training and experience satisfy the requirements the sponsor has established. A health professional who is not an investigator may in some instances use a device under the supervision of an investigator.

Monitoring investigations (812.46)

Q. Must IDE investigations be monitored? Who has this responsibility?

A. Yes, and sponsors are responsible for ensuring proper monitoring of investigations. This generally includes:

- ensuring that investigators follow signed investigator agreements;
- evaluating immediately unanticipated adverse effects, and reporting the results to FDA;
- securing compliance of devices or, if necessary, discontinuing their shipment to investigators; and
- ensuring that unused devices are disposed of properly.

Q. What are the responsibilities of a manufacturer who discovers a physician conducting a clinical investigation of a significant risk device for a use other than the use for which the device may legally be commercially distributed?

A. In this instance, the physician would be considered a sponsor-investigator and would be responsible for obtaining an approved IDE. The manufacturer should stop shipping the device unless the manufacturer informs the physician to submit an IDE application.

Q. If an investigator continues to use a significant risk device after a sponsor has terminated an investigation and has requested that all devices be returned, what steps should the sponsor take?

A. The sponsor should notify FDA and the IRB.

Q. How may a significant risk device investigation that has been terminated be resumed?

A. It may be resumed through the same steps necessary to allow an investigation to begin, i.e., IRB and FDA approvals must be obtained.

Subpart D: IRB Review and Approval (See Part 56, Institutional Review Boards regulation in this chapter)

Subpart E: Responsibilities of Investigators

Specific responsibilities of investigators (812.110)

Q. What must be done with unused devices at the end of a significant risk device investigation?

A. They must be returned to the sponsor or otherwise disposed of as the sponsor directs.

Subpart F: Reserved

Subpart G: Records and Reports

Records (812.140)

Q. If a device investigation is exempt from the IDE regulation, are there other recordkeeping requirements that the sponsor or device manufacturer must meet?

A. If the device is not in commercial distribution, there are no recordkeeping requirements. If it is in commercial distribution, the manufacturer must comply with the recordkeeping requirements of the Act, e.g., GMP recordkeeping requirements.

Inspections (812.145)

Q. Are there IDE compliance programs established to inspect records of an investigation?

A. Yes. Under the Bioresearch Monitoring Program, FDA inspects sponsors, monitors, IRBs, and investigators. The specific compliance programs are: 7378.808 - Good Laboratory Practice Program, Non-Clinical Laboratories; 7378.809 - Institutional Review Board Program; 7378.810 - Sponsor/Monitor Program; and 7378.811A - Clinical Investigators Followup. They are currently available from FDA upon request through FOI.

Q. When FDA inspects an investigator at an institution, is the institution's approval required?

A. No. It is not necessary for the clinical investigator to obtain approval from the institution before permitting an FDA inspection. The institution, however, will be notified by FDA that an inspection is pending. Inspections will be conducted during normal business hours and the FDA investigators will identify themselves and present their credentials. It may be necessary for the clinical investigator to obtain permission from the institution to take the FDA investigator to a portion of the institution where the clinical investigator may not have access.

Reports (812.150)

Q. Must an IRB be notified if an emergency change is made in the investigational plan to protect the life or physical well-being of a subject?

A. Yes. The sponsor and the reviewing IRB must be notified no later than 5 working days after the emergency occurred. Nonemergency changes require prior FDA and IRB approval in accordance with 812.35(a).

Q. Will a sponsor be subject to administrative sanctions for failing to make the proper notifications to FDA, IRBs, and others? If so, what penalties may be involved?

A. Yes. The penalties would vary depending on the nature of the violation (e.g., failure to make a notification, falsification of a report, or an incomplete report). The reason for the violation, and the importance of the item will be addressed in FDA's notification to the sponsor. Penalties could vary widely from withdrawal of approval of investigations to criminal prosecution.

Q. If an investigation is being reviewed by several IRBs, must the sponsor send progress reports of the investigation to all reviewing IRBs?

A. Yes.

Q. What kind of information is required in progress reports and in final reports?

A. The IDE regulation does not specify the kind of information required in progress reports, but they generally should contain information specified by IRBs to enable them to review progress. In addition, FDA has a guidance on "Suggested Format for IDE Progress Reports" included in this chapter. FDA uses this as a checklist in their review of progress reports and the format for final reports.

Q. A sponsor presents an investigation to several IRBs and explains that the device is a nonsignificant risk device. Some of the IRBs agree, but other IRBs believe it is a significant risk device. May the sponsor begin the investigation at those institutions at which IRBs agreed with the nonsignificant risk determination?

A. Technically, yes. The IDE regulation requires, however, that the sponsor report to FDA those instances in which IRBs determined the device to be a significant risk device. FDA recommends the sponsor request FDA's guidance before initiating the investigation in the situation described. FDA makes its determination on a case-by-case basis.

Part 50: Informed Consent of Human Subjects Regulation

Q. What are the responsibilities of the investigator, sponsor, and IRB for ensuring adequate informed consent?

A. For either significant or nonsignificant risk device investigations, the investigator must obtain and document informed consent in accordance with 50.27. The investigator must document use of a device without informed consent and must report such use to the sponsor and the reviewing IRB within 5 working days after the occurrence.

The sponsor must ensure that adequate informed consent is obtained and must provide FDA with a copy of any report of device use without informed consent within 5 working days of receiving such a report. The sponsor of a significant risk device investigation must submit, as part of the IDE application, copies of all forms and informational materials to be provided to subjects in obtaining informed consent.

The IRB must judge the adequacy of informed consent documents and should disapprove an investigation or withdraw approval if informed consent is inadequate.

Q. If no IRB exists or a sponsor cannot find an IRB willing to review the sponsor's investigation, may an independent IRB or group be established outside an academic or health care institution?

A. Yes. Some situations might require establishing an independent IRB. For example, a sponsor might use investigators not affiliated with an institution; an investigation might be conducted in physicians' offices; or manufacturers might conduct investigations using their own facilities with their employees as subjects.

FDA recommends that the sponsor first attempt to contract with a commercial testing laboratory or a contract research organization to establish an IRB. If unable to contract for IRB review, the sponsor may establish an IRB. If unable to establish an independent IRB by either of these methods, the sponsor may submit documentation of these efforts to obtain IRB review and may request FDA to review the application without previous IRB review.

Q. In lieu of an IRB, will FDA review investigations?

A. Under only the most unusual circumstances does FDA intend to perform patient risk reviews. It is difficult for FDA to perform these reviews because of the need to apply local community standards in reviewing the acceptability of risks associated with clinical investigations.

Q. May a sponsor financially assist an IRB?

A. Yes. A sponsor may provide financial support for reasonable administrative assistance, such as clerical assistance.

Q. Must an IRB have a general assurance number?

A. No, not for an IRB to review a clinical investigation of a medical device. It is required, however, if an institution seeks DHHS funding. Further information on general assurance numbers is available from the Office for Protection from Research Risks, National Institutes of Health, Bethesda, MD 20014.

Q. May an institution have more than one IRB?

A. Yes, but this would be unusual. IRBs are committees established by an institution according to its own policies and needs.

Q. How does the sponsor protect confidential information submitted to an IRB?

A. The sponsor should designate in the IDE application any information the sponsor believes to be proprietary. A sponsor may wish to negotiate with the institution an agreement in which the institution assures that the IRB members have been advised of the data's proprietary nature and that the IRB members will not disclose any such information.

Q. Who is responsible for the selection of IRB members?

A. The regulation does not specifically address this responsibility. The administration of the institution at which the IRB functions is responsible for the selection process. IRB membership should meet the criteria listed in 56.107.

Q. If an institution has requirements that conflict with FDA's IDE requirements, which requirements prevail?

A. FDA's IDE requirements will prevail, unless FDA grants a waiver. An institution may impose conditions for conducting a study that are additional to FDA requirements, but an institution may not alter, delete, or lessen FDA requirements.

Q. Who is responsible for monitoring the composition and continuing performance of IRBs?

A. Institutions have the primary responsibility for this, but FDA must ensure that IRBs operate in accordance with Part 56, the IRB regulation, which became effective July 27, 1981. IRBs that review significant risk device investigations are inspected as part of the FDA Bioresearch Monitoring Program. Many of these IRBs review nonsignificant risk device investigations, and FDA may also examine these reviews as part of the Bioresearch Monitoring Program.

Q. What does the term "scientific soundness" mean?

A. This refers to an assessment by an IRB or by FDA about the design of a clinical investigation. A judgment that an investigation is scientifically sound reflects, among other things, that the investigation has specific and well-defined objectives and that it has the potential to yield useful knowledge that warrants exposing patients to the specific risks involved.

Q. May an institution subject an investigation to several types of review in addition to IRB review, e.g., peer or departmental review?

A. Yes. An institution may properly withhold approval of an investigation until the protocol has undergone a multifaceted review. FDA requires only that the sponsor certify IRB approval. An institution may require more extensive review if it decides this is required for patient protection or for any other reason. The IRB serves, however, as the spokesperson for the institution on patient protection. Under the IRB regulation, an institution may not overrule an IRB disapproval.

Q. How does FDA interpret the term "commence" for purposes of applicability of the IRB regulations?

A. A clinical investigation "commences" on the date an application for an IDE or IDE supplement is received by FDA or by an IRB, as required. Thus, an IRB reviewing an IDE or IDE supplement received on or after July 27, 1981, must be in compliance with the IRB regulations.

Q. Are the manufacturers, specification developers or sponsors of a radiation-emitting electronic product(s), with an IDE, exempt from performance standards and submitting initial reports?

A. The requirements of the Radiation Control Health and Safety Act and performance standards are not affected by an IDE. Certification and initial reporting before products are used on patients is still required.

Other Questions

Q. Can a sponsor compensate an investigator without creating a conflict of interest?

A. Yes. The compensation of an investigator by a sponsor is not considered conflict of interest.

Q. Who decides if a device is ineffective?

A. FDA makes the determination if a device should be approved for marketing as part of its review of safety and effectiveness data. An IRB, a sponsor, or FDA may decide to terminate an investigation prior to its scheduled completion if there is reason to believe that the device is ineffective or unsafe.

Q. In an emergency, is FDA approval required before shipping an investigational device to an investigator, if that investigator is not part of the investigation or if there is no approved IDE for the investigation?

A. No. FDA allows an investigational device to be used in a true emergency situation if the manufacturer, the investigator, and the institution or its IRB approve the emergency use. FDA requests notification from the sponsor when an investigational device has been used in this way.

Q. After completing a clinical investigation in accordance with the IDE regulation, what must be done to obtain FDA approval to market the device?

A. If a device manufacturer believes, according to data obtained from the investigation, that the device is substantially equivalent to a preamendment device, then the manufacturer should submit a premarket notification known as a 510(k) to FDA. If FDA determines the device to be substantially equivalent, it may be marketed. Devices determined not to be substantially equivalent are automatically placed in Class III and must undergo premarket approval or be reclassified into Class I or Class II before they may be marketed.

A BRIEF SUMMARY OF THE GOOD LABORATORY PRACTICE REGULATIONS

The Good Laboratory Practice Regulations prescribe good laboratory practices for conducting nonclinical laboratory studies designed to support applications for research or market permits for a number of FDA regulated products, including medical devices for human use.

Nonclinical laboratory studies include any in vivo or in vitro experiments in which a test article is studied in a test system under laboratory conditions to determine its safety. The term "nonclinical laboratory studies" does not include:

- clinical studies, or studies involving human subjects; or
- basic exploratory studies conducted to determine the chemical or physical characteristics of a test article, or whether it has any potential utility.

In the case of medical devices, applications for research or marketing permits involving safety data may include:

- an application for an investigation device exemption (Part 812);
- an application for premarket approval of a medical device (Section 515 of the Act);
- a product development protocol for a medical device (Section 515 of the Act); and
- data and information on a medical device submitted as part of required procedures for classifying it (Section 513 of the Act), or for establishing a performance standard or requesting a variance or exemption from a performance standard (Section 514 of the Act).

PART 812—INVESTIGATIONAL DEVICE EXEMPTIONS

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SOURCE: 45 FR 3751, Jan. 18, 1980, unless otherwise noted.

Subpart A—General Provisions

§ 812.1 Scope.

(a) The purpose of this part is to encourage, to the extent consistent with the protection of public health and safety and with ethical standards, the discovery and development of useful devices intended for human use, and to that end to maintain optimum freedom for scientific investigators in their pursuit of this purpose. This part provides procedures for the conduct of clinical investigations of devices. An approved investigational device exemption (IDE) permits a device that otherwise would be required to comply with a performance standard or to have premarket approval to be shipped lawfully for the purpose of conducting investigations of that device. An IDE approved under § 812.30 or considered approved under § 812.2(b) exempts a device from the requirements of the following sections of the act and regulations issued thereunder: Misbranding under section 502, registration, listing, and premarket notification under section 510, performance standards under section 514, premarket approval under section 515, a banned device regulation under section 516, records and reports under section 519, restricted device requirements under section 520(e), good manufacturing practice requirements under section 520(f) (unless the sponsor states an intention to comply with these requirements under § 812.20(b)(3) or § 812.140(b)(4)(v)) and color additive requirements under section 706.

(b) References in this part to regulatory sections of the Code of Federal Regulations are to Chapter I of Title 21, unless otherwise noted.

§ 812.2 Applicability.

(a) *General.* This part applies to all clinical investigations of devices to determine safety and effectiveness, except as provided in paragraph (c) of this section.

(b) *Abbreviated requirements.* The following categories of investigations are considered to have approved applications for IDE's, unless FDA has notified a sponsor under § 812.20(a) that approval of an application is required:

(1) An investigation of a device other than a significant risk device, if the device is not a banned device and the sponsor:

(i) Labels the device in accordance with § 812.5;

(ii) Obtains IRB approval of the investigation after presenting the reviewing IRB with a brief explanation of why the device is not a significant risk device, and maintains such approval;

(iii) Ensures that each investigator participating in an investigation of the device obtains from each subject under the investigator's care, informed consent under Part 50 and documents it, unless documentation is waived by an IRB under § 56.109(c).

(iv) Complies with the requirements of § 812.46 with respect to monitoring investigations;

(v) Maintains the records required under § 812.140(b) (4) and (5) and makes the reports required under § 812.150(b) (1) through (3) and (5) through (10);

(vi) Ensures that participating investigators maintain the records required by § 812.140(a)(3)(i) and make the reports required under § 812.150(a) (1), (2), (5), and (7); and

(vii) Complies with the prohibitions in § 812.7 against promotion and other practices.

(2) An investigation of a device other than one subject to paragraph (e) of this section, if the investigation was begun on or before July 16, 1980, and to be completed, and is completed, on or before January 19, 1981.

(c) *Exempted investigations.* This part does not apply to investigations of the following categories of devices:

(1) A device, other than a transitional device, in commercial distribution immediately before May 28, 1976, when used or investigated in accordance with the indications in labeling in effect at that time.

(2) A device, other than a transitional device, introduced into commercial distribution on or after May 28, 1976, that FDA has determined to be substantially equivalent to a device in commercial distribution immediately before May 28, 1976, and that is used or investigated in accordance with the indications in the labeling FDA reviewed under Subpart E of Part 807 in determining substantial equivalence.

(3) A diagnostic device, if the sponsor complies with applicable requirements in § 809.10(c) and if the testing:

(i) Is noninvasive,

(ii) Does not require an invasive sampling procedure that presents significant risk,

(iii) Does not by design or intention introduce energy into a subject, and

(iv) Is not used as a diagnostic procedure without confirmation of the diagnosis by another, medically established diagnostic product or procedure.

(4) A device undergoing consumer preference testing, testing of a modification, or testing of a combination of two or more devices in commercial distribution, if the testing is not for the purpose of determining safety or effectiveness and does not put subjects at risk.

(5) A device intended solely for veterinary use.

(6) A device shiped solely for research on or with laboratory animals and labeled in accordance with § 812.5(c).

(7) A custom device as defined in § 812.3(b), unless the device is being used to determine safety or effectiveness for commercial distribution.

(8) An intraocular lens. An intraocular lens shall not be used unless it is subject to an approved IDE under Part 813 or an approved application for premarket approval under section 515 of the act.

(d) *Limit on certain exemptions.* In the case of class II or class III device described in paragraph (c)(1) or (2) of this section, this part applies beginning on the date stipulated in an FDA regulation or order that calls for the submission of premarket approval applications for an unapproved class III device, or establishes a performance standard for a class II device.

(e) *Investigations subject to IND's.* A sponsor that, on July 16, 1980, has an effective investigational new drug exemption (IND) for an investigation of a device shall continue to comply with the requirements of Part 312 until 90 days after that date. To continue the investigation after that date, a sponsor shall comply with paragraph (b)(1) of this section, if the device is not a significant risk device, or shall have obtained FDA approval under § 812.30 of an IDE application for the investigation of the device.

(Secs. 406, 408, 409, 502, 503, 505, 506, 507, 510, 513-516, 518-520, 701(a), 706, and 801, 52 Stat. 1049-1053 as amended, 1055, 1058 as amended, 55 Stat 851 as amended, 59 Stat. 463 as amended, 68 Stat. 511-517 as amended, 72 Stat. 1785-1788 as amended, 74 Stat. 399-407 as amended, 76 Stat. 794-795 as amended, 90 Stat. 540-560, 562-574 (21 U.S.C. 346, 346a, 348, 352, 353, 355, 356, 357, 360, 360c-360f, 360h-360j, 371(a), 376 and 381); secs. 215, 301, 351, 354-360F, 58 Stat. 690, 702 as amended, 82 Stat. 1173-1186 as amended (42 U.S.C. 216, 241, 262, 263b-263n))

[45 FR 3751, Jan. 18, 1980, as amended at 46 FR 8956, Jan. 27, 1981; 46 FR 14340, Feb. 27, 1981]

§ 812.3 Definitions.

(a) "Act" means the Federal Food, Drug, and Cosmetic Act (sections 201-901, 52 Stat. 1040 et seq., as amended (21 U.S.C. 301-392)).

(b) "Custom device" means a device that:

(1) Necessarily deviates from devices generally available or from an applicable performance standard or premarket approval requirement in order to comply with the order of an individual physician or dentist;

(2) Is not generally available to, or generally used by, other physicians or dentists;

(3) Is not generally available in finished form for purchase or for dispensing upon prescription;

(4) Is not offered for commercial distribution through labeling or advertising; and

(5) Is intended for use by an individual patient named in the order of a physician or dentist, and is to be made in a specific form for that patient, or is intended to meet the special needs of the physician or dentist in the course of professional practice.

(c) "FDA" means the Food and Drug Administration.

(d) "Implant" means a device that is placed into a surgically or naturally formed cavity of the human body if it is intended to remain there for a period of 30 days or more. FDA may, in order to protect public health, determine that devices placed in subjects for shorter periods are also "implants" for purposes of this part.

(e) "Institution" means a person, other than an individual, who engages in the conduct of research on subjects or in the delivery of medical services to individuals as a primary activity or as an adjunct to providing residential or custodial care to humans. The term includes, for example, a hospital, retirement home, confinement facility, academic establishment, and device manufacturer. The term has the same meaning as "facility" in section 520(g) of the act.

(f) "Institutional review board" (IRB) means any board, committee, or other group formally designated by an institution to review biomedical research involving subjects and established, operated, and functioning in conformance with Part 56. The term has the same meaning as "institutional review committee" in section 520(g) of the act.

(g) "Investigational device" means a device, including a transitional device, that is the object of an investigation.

(h) "Investigation" means a clinical investigation or research involving one or more subjects to determine the safety or effectiveness of a device.

(i) "Investigator" means an individual who actually conducts a clinical investigation, i.e., under whose immediate direction the test article is administered or dispensed to, or used involving, a subject, or, in the event of an investigation conducted by a team of individuals, is the responsible leader of that team.

(j) "Monitor," when used as a noun, means an individual designated by a sponsor or contract research organization to oversee the progress of an investigation. The monitor may be an employee of a sponsor or a consultant to the sponsor, or an employee of or consultant to a contract research organization. "Monitor," when used as a verb, means to oversee an investigation.

(k) "Noninvasive," when applied to a diagnostic device or procedure, means one that does not by design or intention: (1) Penetrate or pierce the skin or mucous membranes of the body, the ocular cavity, or the urethra, or (2) enter the ear beyond the external auditory canal, the nose beyond the nares, the mouth beyond the pharynx, the anal canal beyond the rectum, or the vagina beyond the cervical os. For purposes of this part, blood sampling that involves simple venipuncture is considered noninvasive, and the use of surplus samples of body fluids or tissues that are left over from samples taken for noninvestigational purposes is also considered noninvasive.

(l) "Person" includes any individual, partnership, corporation, association, scientific or academic establishment, Government agency or organizational unit of a Government agency, and any other legal entity.

(m) "Significant risk device" means an investigational device that:

(1) Is intended as an implant and presents a potential for serious risk to the health, safety, or welfare of a subject;

(2) Is purported or represented to be for a use in supporting or sustaining human life and presents a potential for serious risk to the health, safety, or welfare of a subject;

(3) Is for a use of substantial importance in diagnosing, curing, mitigating, or treating disease, or otherwise preventing impairment of human health and presents a potential for serious risk to the health, safety, or welfare of a subject; or

(4) Otherwise presents a potential for serious risk to the health, safety, or welfare of a subject.

(n) "Sponsor" means a person who initiates, but who does not actually conduct, the investigation, that is, the investigational device is administered, dispensed, or used under the immediate direction of another individual. A person other than an individual that uses one or more of its own employees to conduct an investigation that it has initiated is a sponsor, not a sponsor-investigator, and the employees are investigators.

(o) "Sponsor-investigator" means an individual who both initiates and actually conducts, alone or with others, an investigation, that is, under whose immediate direction the investigational device is administered, dispensed, or used. The term does not include any person other than an individual. The obligations of a sponsor-investigator under this part include those of an investigator and those of a sponsor.

(p) "Subject" means a human who participates in an investigation, either as an individual on whom or on whose specimen an investigational device is used or as a control. A subject may be in normal health or may have a medical condition or disease.

(q) "Termination" means a discontinuance, by sponsor or by withdrawal of IRB or FDA approval, of an investigation before completion.

(r) "Transitional device" means a device subject to section 520(l) of the act, that is, a device that FDA considered to be a new drug or an antibiotic drug before May 28, 1976.

(s) "Unanticipated adverse device effect" means any serious adverse effect on health or safety or any life-threatening problem or death caused by, or associated with, a device, if that effect, problem, or death was not previously identified in nature, severity, or degree of incidence in the investigational plan or application (including a supplementary plan or application), or any other unanticipated serious problem associated with a device that relates to the rights, safety, or welfare of subjects.

(Secs. 406, 408, 409, 502, 503, 505, 506, 507, 510, 513-516, 518-520, 701(a), 706, and 801, 52 Stat. 1049-1053 as amended, 1055, 1058 as amended, 55 Stat 851 as amended, 59 Stat. 463 as amended, 68 Stat. 511-517 as amended, 72 Stat. 1785-1788 as amended, 74 Stat. 399-407 as amended, 76 Stat. 794-795 as amended, 90 Stat. 540-560, 562-574 (21 U.S.C. 346, 346a, 348, 352, 353, 355, 356, 357, 360, 360c-360f, 360h-360j, 371(a), 376 and 381); secs. 215, 301, 351, 354-360F, 58 Stat. 690, 702 as amended, 82 Stat. 1173-1186 as amended (42 U.S.C. 216, 241, 262, 263b-263n))

[45 FR 3751, Jan. 18, 1980, as amended at 46 FR 8956, Jan. 27, 1981; 48 FR 15622, Apr. 12, 1983]

§ 812.5 Labeling of investigational devices.

(a) *Contents.* An investigational device or its immediate package shall bear a label with the following information: the name and place of business of the manufacturer, packer, or distributor (in accordance with § 801.1), the quantity of contents, if appropriate, and the following statement: "CAUTION—Investigational device. Limited by Federal (or United States) law to investigational use." The label or other labeling shall describe all relevant contraindications, hazards, adverse effects, interfering substances or devices, warnings, and precautions.

(b) *Prohibitions.* The labeling of an investigational device shall not bear any statement that is false or misleading in any particular and shall not represent that the device is safe or effective for the purposes for which it is being investigated.

(c) *Animal research.* An investigational device shipped solely for research on or with laboratory animals shall bear on its label the following statement: "CAUTION—Device for investigational use in laboratory animals or other tests that do not involve human subjects."

[45 FR 3751, Jan. 18, 1980, as amended at 45 FR 58842, Sept. 5, 1980]

§ 812.7 Prohibition of promotion and other practices.

A sponsor, investigator, or any person acting for or on behalf of a sponsor or investigator shall not:

(a) Promote or test market an investigational device, until after FDA has approved the device for commercial distribution.

(b) Commercialize an investigational device by charging the subjects or investigators for a device a price larger than that necessary to recover costs of manufacture, research, development, and handling.

(c) Unduly prolong an investigation. If data developed by the investigation indicate in the case of a class III device that premarket approval cannot be justified or in the case of a class II device that it will not comply with an applicable performance standard or an amendment to that standard, the sponsor shall promptly terminate the investigation.

(d) Represent that an investigational device is safe or effective for the purposes for which it is being investigated.

§ 812.10 Waivers.

(a) *Request.* A sponsor may request FDA to waive any requirement of this part. A waiver request, with supporting documentation, may be submitted separately or as part of an application to the address in § 812.19.

(b) *FDA action.* FDA may by letter grant a waiver of any requirement that FDA finds is not required by the act and is unnecessary to protect the rights, safety, or welfare of human subjects.

(c) *Effect of request.* Any requirement shall continue to apply unless and until FDA waives it.

§ 812.18 Import and export requirements.

(a) *Imports.* In addition to complying with other requirements of this part, a person who imports or offers for importation an investigational device subject to this part shall be the agent of the foreign exporter with respect to investigations of the device and shall act as the sponsor of the clinical investigation, or ensure that another person acts as the agent of the foreign exporter and the sponsor of the investigation.

(b) *Exports.* A person exporting an investigational device subject to this part shall obtain FDA's prior approval, as required by section 801(d) of the act.

§ 812.19 Address for IDE correspondence.

All applications, supplemental applications, reports, requests for waivers, requests for import or export approval, and other correspondence relating to matters covered by this part shall be addressed to the Bureau of Medical Devices, Document Control Center (HFK-20), Food and Drug Administration, 8757 Georgia Ave., Silver Spring, MD 20910. The outside wrapper of each submission shall state what the submission is, for example an "IDE application," a "supplemental IDE application," or "correspondence concerning an IDE (or an IDE application)."

Subpart B—Application and Administrative Action

§ 812.20 Application.

(a) *Submission.* (1) A sponsor shall submit an application to FDA if the sponsor intends to use a significant risk device in an investigation or if FDA notifies the sponsor that an application is required for an investigation.

(2) A sponsor shall not begin an investigation for which FDA's approval of an application is required until FDA has approved the application.

(3) A sponsor shall submit three copies of a signed "Application for an Investigational Device Exemption" (IDE application), together with accompanying materials, by registered mail or by hand to the address in § 812.19. Subsequent correspondence concerning an application or a supplemental application shall be submitted by registered mail or by hand.

(b) *Contents.* An IDE application shall include, in the following order:

(1) The name and address of the sponsor.

(2) A complete report of prior investigations of the device and an accurate summary of those sections of the investigational plan described in § 812.25(a) through (e) or, in lieu of the summary, the complete plan. The sponsor shall submit to FDA a complete investigational plan and a complete report of prior investigations of the device if no IRB has reviewed them, if FDA has found an IRB's review inadequate, or if FDA requests them.

(3) A description of the methods, facilities, and controls used for the manufacture, processing, packing, storage, and, where appropriate, installation of the device, in sufficient detail so that a person generally familiar with good manufacturing practices can make a knowledgeable judgment about the quality control used in the manufacture of the device.

(4) An example of the agreements to be entered into by all investigators to comply with investigator obligations under this part, and a list of the names and addresses of all investigators who have signed the agreement.

(5) A certification that all investigators who will participate in the investigation have signed the agreement, that the list of investigators includes all the investigators participating in the investigation, and that no investigators will be added to the investigation until they have signed the agreement.

(6) A list of the name, address, and chairperson of each IRB that has been or will be asked to review the investigation and a certification of the action concerning the investigation taken by each such IRB.

(7) The name and address of any institution at which a part of the investigation may be conducted that has not been identified in accordance with paragraph (b)(6) of this section.

(8) If the device is to be sold, the amount to be charged and an explanation of why sale does not constitute commercialization of the device.

(9) A claim for categorical exclusion under § 25.24 of this chapter or an environmental assessment under § 25.31 of this chapter.

(10) Copies of all labeling for the device.

(11) Copies of all forms and informational materials to be provided to subjects to obtain informed consent.

(12) Any other relevant information FDA requests for review of the application.

(c) *Additional information.* FDA may request additional information concerning an investigation or revision in the investigational plan. The sponsor may treat such a request as a disapproval of the application for purposes of requesting a hearing under Part 16.

(d) *Information previously submitted.* Information previously submitted to the Bureau of Medical Devices in accordance with this chapter ordinarily need not be resubmitted, but may be incorporated by reference.

(Secs. 406, 408, 409, 502, 503, 505, 506, 507, 510, 513-516, 518-520, 701(a), 706, and 801, 52 Stat. 1049-1053 as amended, 1055, 1058 as amended, 55 Stat 851 as amended, 59 Stat. 463 as amended, 68 Stat. 511-517 as amended, 72 Stat. 1785-1788 as amended, 74 Stat. 399-407 as amended, 76 Stat. 794-795 as amended, 90 Stat. 540-560, 562-574 (21 U.S.C. 346, 346a, 348, 352, 353, 355, 356, 357, 360, 360c-360f, 360h-360j, 371(a), 376 and 381); secs. 215, 301, 351, 354-360F, 58 Stat. 690, 702 as amended, 82 Stat. 1173-1186 as amended (42 U.S.C. 216, 241, 262, 263b-263n))

[45 FR 3751, Jan. 18, 1980, as amended at 46 FR 8956, Jan. 27, 1981; 50 FR 16669, Apr. 26, 1985]

§ 812.25 Investigational plan.

The investigational plan shall include, in the following order:

(a) *Purpose.* The name and intended use of the device and the objectives and duration of the investigation.

(b) *Protocol.* A written protocol describing the methodology to be used and an analysis of the protocol demonstrating that the investigation is scientifically sound.

(c) *Risk analysis.* A description and analysis of all increased risks to which subjects will be exposed by the investigation; the manner in which these risks will be minimized; a justification for the investigation; and a description of the patient population, including the number, age, sex, and condition.

(d) *Description of device.* A description of each important component, ingredient, property, and principle of operation of the device and of each anticipated change in the device during the course of the investigation.

(e) *Monitoring procedures.* The sponsor's written procedures for monitoring the investigation and the name and address of any monitor.

(f) *Labeling.* Copies of all labeling for the device.

(g) *Consent materials.* Copies of all forms and informational materials to be provided to subjects to obtain informed consent.

(h) *IRB information.* A list of the names, locations, and chairpersons of all IRB's that have been or will be asked to review the investigation, and a certification of any action taken by any of those IRB's with respect to the investigation.

(i) *Other institutions.* The name and address of each institution at which a part of the investigation may be conducted that has not been identified in paragraph (h) of this section.

(j) *Additional records and reports.* A description of records and reports that will be maintained on the investigation in addition to those prescribed in Subpart G.

§ 812.27 Report of prior investigations.

(a) *General.* The report of prior investigations shall include reports of all prior clinical, animal, and laboratory testing of the device and shall be comprehensive and adequate to justify the proposed investigation.

(b) *Specific contents.* The report also shall include:

(1) A bibliography of all publications, whether adverse or supportive, that are relevant to an evaluation of the safety or effectiveness of the device, copies of all published and unpublished adverse information, and, if requested by an IRB or FDA, copies of other significant publications.

(2) A summary of all other unpublished information (whether adverse or supportive) in the possession of, or reasonably obtainable by, the sponsor that is relevant to an evaluation of the safety or effectiveness of the device.

(3) If information on nonclinical laboratory studies is provided, a statement that all such studies have been conducted in compliance with applicable requirements in the good laboratory practice regulations in Part 58, or if any such study was not conducted in compliance with such regulations, a brief statement of the reason for the noncompliance. Failure or inability to comply with this requirement does not justify failure to provide information on a relevant nonclinical test study.

[45 FR 3751, Jan. 18, 1980, as amended at 50 FR 7518, Feb. 22, 1985]

§ 812.30 FDA action on applications.

(a) *Approval or disapproval.* FDA will notify the sponsor in writing of the date it receives an application. FDA may approve an investigation as proposed, approve it with modifications, or disapprove it. An investigation may not begin until:

(1) Thirty days after FDA receives the application at the address in § 812.19 for the investigation of a device other than a banned device, unless FDA notifies the sponsor that the investigation may not begin; or

(2) FDA approves, by order, an IDE for the investigation.

(b) *Grounds for disapproval or withdrawal.* FDA may disapprove or withdraw approval of an application if FDA finds that:

(1) There has been a failure to comply with any requirement of this part or the act, any other applicable regulation or statute, or any condition of approval imposed by an IRB or FDA.

(2) The application or a report contains an untrue statement of a material fact, or omits material information required by this part.

(3) The sponsor fails to respond to a request for additional information within the time prescribed by FDA.

(4) There is reason to believe that the risks to the subjects are not outweighed by the anticipated benefits to the subjects and the importance of the knowledge to be gained, or informed consent is inadquate, or the investigation is scientifically unsound, or there is reason to believe that the device as used is ineffective.

(5) It is otherwise unreasonable to begin or to continue the investigation owing to the way in which the device is used or the inadequacy of:

(i) The report of prior investigations or the investigational plan;

(ii) The methods, facilities, and controls used for the manufacturing, processing, packaging, storage, and, where appropriate, installation of the device; or

(iii) Monitoring and review of the investigation.

(c) *Notice of disapproval or withdrawal.* If FDA disapproves an application or proposes to withdraw approval of an application, FDA will notify the sponsor in writing.

(1) A disapproval order will contain a complete statement of the reasons for disapproval and a statement that the sponsor has an opportunity to request a hearing under Part 16.

(2) A notice of a proposed withdrawal of approval will contain a complete statement of the reasons for withdrawal and a statement that the sponsor has an opportunity to request a hearing under Part 16. FDA will provide the opportunity for hearing before withdrawal of approval, unless FDA determines in the notice that continuation of testing under the exemption will result in an unreasonble risk to the public health and orders withdrawal of approval before any hearing.

[45 FR 3751, Jan. 18, 1980, as amended at 45 FR 58842, Sept. 5, 1980]

§ 812.35 Supplemental applications.

(a) *Changes in investigational plan.* A sponsor shall: (1) Submit to FDA a supplemental application if the sponsor or an investigator proposes a change in the investigational plan that may affect its scientific soundness or the rights, safety, or welfare of subjects, and (2) obtain FDA approval under § 812.30(a) of any such change, and IRB approval when the change involves the rights, safety, or welfare of subjects (see §§ 56.110 and 56.111), before implementation. These requirements do not apply in the case of a deviation from the investigational plan to protect the life or physical wellbeing of a subject in an emergency, which deviation shall be reported to FDA within 5 working days after the sponsor learns of it (see § 812.150(a)(4)).

(b) *IRB approval for new facilities.* A sponsor shall submit to FDA a certification of any IRB approval of an investigation or a part of an investigation not included in the IDE application. If the investigation is otherwise unchanged, the supplemental application shall consist of an updating of the information required by § 812.20(b) and (c) and a description of any modifications in the investigational plan required by the IRB as a condition of approval. A certification of IRB approval need not be included in the initial submission of the supplemental application, and such certification is not a precondition for agency consideration of the application. Nevertheless, a sponsor may not begin a part of an investigation at a facility until the IRB has approved the investigation, FDA has received the certification of IRB approval, and FDA, under § 812.30(a), has approved the supplemental application relating to that part of the investigation (see § 56.103(a)).

[50 FR 25909, June 24, 1985; 50 FR 28932, July 17, 1985]

§ 812.38 Confidentiality of data and information.

(a) *Existence of IDE.* FDA will not disclose the existence of an IDE unless its existence has previously been publicly disclosed or acknowledged, until FDA approves an application for premarket approval of the device subject to the IDE; or a notice of completion of a product development protocol for the device has become effective.

(b) *Availability of summaries or data.* (1) FDA will make publicly available, upon request, a detailed summary of information concerning the safety and effectiveness of the device that was the basis for an order approving, disapproving, or withdrawing approval of an application for an IDE for a banned device. The summary shall include information on any adverse effect on health caused by the device.

(2) If a device is a banned device or if the existence of an IDE has been publicly disclosed or acknowledged, data or information contained in the file is not available for public disclosure before approval of an application for premarket approval or the effective date of a notice of completion of a product development protocol except as provided in this section. FDA may, in its discretion, disclose a summary of selected portions of the safety and effectiveness data, that is, clinical, animal, or laboratory studies and tests of the device, for public consideration of a specific pending issue.

(3) If the existence of an IDE file has not been publicly disclosed or acknowledged, no data or information in the file are available for public disclosure except as provided in paragraphs (b)(1) and (c) of this section.

(c) *Reports of adverse effects.* Upon request or on its own initiative, FDA shall disclose to an individual on whom an investigational device has been used a copy of a report of adverse device effects relating to that use.

(d) *Other rules.* Except as otherwise provided in this section, the availability for public disclosure of data and information in an IDE file shall be handled in accordance with § 314.14, which concerns the confidentiality of data and information in new drug applications, until the effective date of regulations concerning the confidentiality of data and information in applications for premarket approval of devices.

Subpart C—Responsibilities of Sponsors

§ 812.40 General responsibilities of sponsors.

Sponsors are responsible for selecting qualified investigators and providing them with the information they need to conduct the investigation properly, ensuring proper monitoring of the investigation, ensuring that IRB review and approval are obtained, submitting an IDE application to FDA, and ensuring that any reviewing IRB and FDA are promptly informed of significant new information about an investigation. Additional responsibilities of sponsors are described in Subparts B and G.

§ 812.42 FDA and IRB approval.

A sponsor shall not begin an investigation or part of an investigation until an IRB and FDA have both approved the application or supplemental application relating to the investigation or part of an investigation.

(Secs. 406, 408, 409, 502, 503, 505, 506, 507, 510, 513-516, 518-520, 701(a), 706, and 801, 52 Stat. 1049-1053 as amended, 1055, 1058 as amended, 55 Stat 851 as amended, 59 Stat. 463 as amended, 68 Stat. 511-517 as amended, 72 Stat. 1785-1788 as amended, 74 Stat. 399-407 as amended, 76 Stat. 794-795 as amended, 90 Stat. 540-560, 562-574 (21 U.S.C. 346, 346a, 348, 352, 353, 355, 356, 357, 360, 360c-360f, 360h-360j, 371(a), 376 and 381); secs. 215, 301, 351, 354-360F, 58 Stat. 690, 702 as amended, 82 Stat. 1173-1186 as amended (42 U.S.C. 216, 241, 262, 263b-263n))

[46 FR 8957, Jan. 27, 1981]

§ 812.43 Selecting investigators and monitors.

(a) *Selecting investigators.* A sponsor shall select investigators qualified by training and experience to investigate the device.

(b) *Control of device.* A sponsor shall ship investigational devices only to qualified investigators participating in the investigation.

(c) *Obtaining agreements.* A sponsor shall obtain from each participating investigator a signed agreement that includes:

(1) The investigator's curriculum vitae.

(2) Where applicable, a statement of the investigator's relevant experience, including the dates, location, extent, and type of experience.

(3) If the investigator was involved in an investigation or other research that was terminated, an explanation of the circumstances that led to termination.

(4) A statement of the investigator's commitment to:

(i) Conduct the investigation in accordance with the agreement, the investigational plan, this part and other applicable FDA regulations, and conditions of approval imposed by the reviewing IRB or FDA;

(ii) Supervise all testing of the device involving human subjects; and

(iii) Ensure that the requirements for obtaining informed consent are met.

(d) *Selecting monitors.* A sponsor shall select monitors qualified by training and experience to monitor the investigational study in accordance with this part and other applicable FDA regulations.

§ 812.45 Informing investigators.

A sponsor shall supply all investigators participating in the investigation with copies of the investigational plan and the report of prior investigations of the device.

§ 812.46 Monitoring investigations.

(a) *Securing compliance.* A sponsor who discovers that an investigator is not complying with the signed agreement, the investigational plan, the requirements of this part or other applicable FDA regulations, or any conditions of approval imposed by the reviewing IRB or FDA shall promptly either secure compliance, or discontinue shipments of the device to the investigator and terminate the investigator's participation in the investigation. A sponsor shall also require such an investigator to dispose of or return the device, unless this action would jeopardize the rights, safety, or welfare of a subject.

(b) *Unanticipated adverse device effects.* (1) A sponsor shall immediately conduct an evaluation of any unanticipated adverse device effect.

(2) A sponsor who determines that an unanticipated adverse device effect presents an unreasonable risk to subjects shall terminate all investigations or parts of investigations presenting that risk as soon as possible. Termination shall occur not later than 5 working days after the sponsor makes this determination and not later than 15 working days after the sponsor first received notice of the effect.

(c) *Resumption of terminated studies.* If the device is a significant risk device, a sponsor may not resume a terminated investigation without IRB and FDA approval. If the device is not a significant risk device, a sponsor may not resume a terminated investigation without IRB approval and, if the investigation was terminated under paragraph (b)(2) of this section, FDA approval.

Subpart D—IRB Review and Approval

§ 812.60 IRB composition, duties, and functions.

An IRB reviewing and approving investigations under this part shall comply with the requirements of Part 56 in all respects, including its composition, duties, and functions.

(Secs. 406, 408, 409, 502, 503, 505, 506, 507, 510, 513-516, 518-520, 701(a), 706, and 801, 52 Stat. 1049-1053 as amended, 1055, 1058 as amended, 55 Stat 851 as amended, 59 Stat. 463 as amended, 68 Stat. 511-517 as amended, 72 Stat. 1785-1788 as amended, 74 Stat. 399-407 as amended, 76 Stat. 794-795 as amended, 90 Stat. 540-560, 562-574 (21 U.S.C. 346, 346a, 348, 352, 353, 355, 356, 357, 360, 360c-360f, 360h-360j, 371(a), 376 and 381); secs. 215, 301, 351, 354-360F, 58 Stat. 690, 702 as amended, 82 Stat. 1173-1186 as amended (42 U.S.C. 216, 241, 262, 263b-263n))

[46 FR 8957, Jan. 27, 1981]

§ 812.62 IRB approval.

(a) An IRB shall review and have authority to approve, require modifications in (to secure approval), or disapprove all investigations covered by this part.

(b) If no IRB exists or if FDA finds that an IRB's review is inadequate, a sponsor may submit an application to FDA.

(Secs. 406, 408, 409, 502, 503, 505, 506, 507, 510, 513-516, 518-520, 701(a), 706, and 801, 52 Stat. 1049-1053 as amended, 1055, 1058 as amended, 55 Stat 851 as amended, 59 Stat. 463 as amended, 68 Stat. 511-517 as amended, 72 Stat. 1785-1788 as amended, 74 Stat. 399-407 as amended, 76 Stat. 794-795 as amended, 90 Stat. 540-560, 562-574 (21 U.S.C. 346, 346a, 348, 352, 353, 355, 356, 357, 360, 360c-360f, 360h-360j, 371(a), 376 and 381); secs. 215, 301, 351, 354-360F, 58 Stat. 690, 702 as amended, 82 Stat. 1173-1186 as amended (42 U.S.C. 216, 241, 262, 263b-263n))

[46 FR 8957, Jan. 27, 1981]

§ 812.64 IRB's continuing review.

The IRB shall conduct its continuing review of an investigation in accordance with Part 56.

(Secs. 406, 408, 409, 502, 503, 505, 506, 507, 510, 513-516, 518-520, 701(a), 706, and 801, 52 Stat. 1049-1053 as amended, 1055, 1058 as amended, 55 Stat 851 as amended, 59 Stat. 463 as amended, 68 Stat. 511-517 as amended, 72 Stat. 1785-1788 as amended, 74 Stat. 399-407 as amended, 76 Stat. 794-795 as amended, 90 Stat. 540-560, 562-574 (21 U.S.C. 346, 346a, 348, 352, 353, 355, 356, 357, 360, 360c-360f, 360h-360j, 371(a), 376 and 381); secs. 215, 301, 351, 354-360F, 58 Stat. 690, 702 as amended, 82 Stat. 1173-1186 as amended (42 U.S.C. 216, 241, 262, 263b-263n))

[46 FR 8957, Jan. 27, 1981]

§ 812.65 [Reserved]

§ 812.66 Significant risk device determinations.

If an IRB determines that an investigation, presented for approval under § 812.2(b)(1)(ii), involves a significant risk device, it shall so notify the investigator and, where appropriate, the sponsor. A sponsor may not begin the investigation except as provided in § 812.30(a).

(Secs. 406, 408, 409, 502, 503, 505, 506, 507, 510, 513-516, 518-520, 701(a), 706, and 801, 52 Stat. 1049-1053 as amended, 1055, 1058 as amended, 55 Stat 851 as amended, 59 Stat. 463 as amended, 68 Stat. 511-517 as amended, 72 Stat. 1785-1788 as amended, 74 Stat. 399-407 as amended, 76 Stat. 794-795 as amended, 90 Stat. 540-560, 562-574 (21 U.S.C. 346, 346a, 348, 352, 353, 355, 356, 357, 360, 360c-360f, 360h-360j, 371(a), 376 and 381); secs. 215, 301, 351, 354-360F, 58 Stat. 690, 702 as amended, 82 Stat. 1173-1186 as amended (42 U.S.C. 216, 241, 262, 263b-263n))

[46 FR 8957, Jan. 27, 1981]

Subpart E—Responsibilities of Investigators

§ 812.100 General responsibilities of investigators.

An investigator is responsible for ensuring that an investigation is conducted according to the signed agreement, the investigational plan and applicable FDA regulations, for protecting the rights, safety, and welfare of subjects under the investigator's care, and for the control of devices under investigation. An investigator also is responsible for ensuring that informed consent is obtained in accordance with Part 50 of this chapter. Additional responsibilities of investigators are described in Subpart G.

(Secs. 406, 408, 409, 502, 503, 505, 506, 507, 510, 513-516, 518-520, 701(a), 706, and 801, 52 Stat. 1049-1053 as amended, 1055, 1058 as amended, 55 Stat 851 as amended, 59 Stat. 463 as amended, 68 Stat. 511-517 as amended, 72 Stat. 1785-1788 as amended, 74 Stat. 399-407 as amended, 76 Stat. 794-795 as amended, 90 Stat. 540-560, 562-574 (21 U.S.C. 346, 346a, 348, 352, 353, 355, 356, 357, 360, 360c-360f, 360h-360j, 371(a), 376 and 381); secs. 215, 301, 351, 354-360F, 58 Stat. 690, 702 as amended, 82 Stat. 1173-1186 as amended (42 U.S.C. 216, 241, 262, 263b-263n))

[45 FR 3751, Jan. 18, 1980, as amended at 46 FR 8957, Jan. 27, 1981]

§ 812.110 Specific responsibilities of investigators.

(a) *Awaiting approval.* An investigator may determine whether potential subjects would be interested in participating in an investigation, but shall not request the written informed consent of any subject to participate, and shall not allow any subject to participate before obtaining IRB and FDA approval.

(b) *Compliance.* An investigator shall conduct an investigation in accordance with the signed agreement with the sponsor, the investigational plan, this part and other applicable FDA regulations, and any conditions of approval imposed by an IRB or FDA.

(c) *Supervising device use.* An investigator shall permit an investigational device to be used only with subjects under the investigator's supervision. An investigator shall not supply an investigational device to any person not authorized under this part to receive it.

(d) *Disposing of device.* Upon completion or termination of a clinical investigation or the investigator's part of an investigation, or at the sponsor's request, an investigator shall return to the sponsor any remaining supply of the device or otherwise dispose of the device as the sponsor directs.

Subpart F—[Reserved]

Subpart G—Records and Reports

§ 812.140 Records.

(a) *Investigator records.* A participating investigator shall maintain the following accurate, complete, and current records relating to the investigator's participation in an investigation:

(1) All correspondence with another investigator, an IRB, the sponsor, a monitor, or FDA, including required reports.

(2) Records of receipt, use or disposition of a device that relate to:

(i) The type and quantity of the device, the dates of its receipt, and the batch number or code mark.

(ii) The names of all persons who received, used, or disposed of each device.

(iii) Why and how many units of the device have been returned to the sponsor, repaired, or otherwise disposed of.

(3) Records of each subject's case history and exposure to the device. Such records shall include:

(i) Documents evidencing informed consent and, for any use of a device by the investigator without informed consent, any written concurrence of a licensed physician and a brief description of the circumstances justifying the failure to obtain informed consent.

(ii) All relevant observations, including records concerning adverse device effects (whether anticipated or unanticipated), information and data on the condition of each subject upon entering, and during the course of, the investigation, including information about relevant previous medical history and the results of all diagnostic tests.

(iii) A record of the exposure of each subject to the investigational device, including the date and time of each use, and any other therapy.

(4) The protocol, with documents showing the dates of and reasons for each deviation from the protocol.

(5) Any other records that FDA requires to be maintained by regulation or by specific requirement for a category of investigations or a particular investigation.

(b) *Sponsor records.* A sponsor shall maintain the following accurate, complete, and current records relating to an investigation:

(1) All correspondence with another sponsor, a monitor, an investigator, an IRB, or FDA, including required reports.

(2) Records of shipment and disposition. Records of shipment shall include the name and address of the consignee, type and quantity of device, date of shipment, and batch number or code mark. Records of disposition shall describe the batch number or code marks of any devices returned to the sponsor, repaired, or disposed of in other ways by the investigator or another person, and the reasons for and method of disposal.

(3) Signed investigator agreements.

(4) For each investigation subject to § 812.2(b)(1) of a device other than a significant risk device, the records described in paragraph (b)(5) of this section and the following records, consolidated in one location and available for FDA inspection and copying:

(i) The name and intended use of the device and the objectives of the investigation;

(ii) A brief explanation of why the device is not a significant risk device:

(iii) The name and address of each investigator:

best copy available

(iv) The name and address of each IRB that has reviewed the investigation:

(v) A statement of the extent to which the good manufacturing practice regulation in Part 820 will be followed in manufacturing the device; and

(vi) Any other information required by FDA.

(5) Records concerning adverse device effects (whether anticipated or unanticipated) and complaints and

(6) Any other records that FDA requires to be maintained by regulation or by specific requirement for a category of investigation or a particular investigation.

(c) *IRB records.* An IRB shall maintain records in accordance with Part 56 of this chapter.

(d) *Retention period.* An investigator or sponsor shall maintain the records required by this subpart during the investigation and for a period of 2 years after the latter of the following two dates: The date on which the investigation is terminated or completed, or the date that the records are no longer required for purposes of supporting a premarket approval application or a notice of completion of a product development protocol.

(e) *Records custody.* An investigator or sponsor may withdraw from the responsibility to maintain records for the period required in paragraph (d) of this section and transfer custody of the records to any other person who will accept responsibility for them under this part, including the requirements of § 812.145. Notice of a transfer shall be given to FDA not later than 10 working days after transfer occurs.

(Secs. 406, 408, 409, 502, 503, 505, 506, 507, 510, 513-516, 518-520, 701(a), 706, and 801, 52 Stat. 1049-1053 as amended, 1055, 1058 as amended, 55 Stat 851 as amended, 59 Stat. 463 as amended, 68 Stat. 511-517 as amended, 72 Stat. 1785-1788 as amended, 74 Stat. 399-407 as amended, 76 Stat. 794-795 as amended, 90 Stat. 540-560, 562-574 (21 U.S.C. 346, 346a, 348, 352, 353, 355, 356, 357, 360, 360c-360f, 360h-360j, 371(a), 376 and 381); secs. 215, 301, 351, 354-360F, 58 Stat. 690, 702 as amended, 82 Stat. 1173-1186 as amended (42 U.S.C. 216, 241, 262, 263b-263n))

[45 FR 3751, Jan. 18, 1980, as amended at 45 FR 58843, Sept. 5, 1980; 46 FR 8957, Jan. 27, 1981]

§ 812.145 Inspections.

(a) *Entry and inspection.* A sponsor or an investigator who has authority to grant access shall permit authorized FDA employees, at reasonable times and in a reasonable manner, to enter and inspect any establishment where devices are held (including any establishment where devices are manufactured, processed, packed, installed, used, or implanted or where records of results from use of devices are kept).

(b) *Records inspection.* A sponsor, IRB, or investigator, or any other person acting on behalf of such a person with respect to an investigation, shall permit authorized FDA employees, at reasonable times and in a reasonable manner, to inspect and copy all records relating to an investigation.

(c) *Records identifying subjects.* An investigator shall permit authorized FDA employees to inspect and copy records that identify subjects, upon notice that FDA has reason to suspect that adequate informed consent was not obtained, or that reports required to be submitted by the investigator to the sponsor or IRB have not been submitted or are incomplete, inaccurate, false, or misleading.

§ 812.150 Reports.

(a) *Investigator reports.* An investigator shall prepare and submit the following complete, accurate, and timely reports:

(1) *Unanticipated adverse device effects.* An investigator shall submit to the sponsor and to the reviewing IRB a report of any unanticipated adverse device effect occurring during an investigation as soon as possible, but in no event later than 10 working days after the investigator first learns of the effect.

(2) *Withdrawal of IRB approval.* An investigator shall report to the sponsor, within 5 working days, a withdrawal of approval by the reviewing IRB of the investigator's part of an investigation.

(3) *Progress.* An investigator shall submit progress reports on the investi-

gation to the sponsor, the monitor, and the reviewing IRB at regular intervals, but in no event less often than yearly.

(4) *Deviations from the investigational plan.* An investigator shall notify the sponsor and the reviewing IRB (see § 56.108(a) (3) and (4)) of any deviation from the investigational plan to protect the life or physical well-being of a subject in an emergency. Such notice shall be given as soon as possible, but in no event later than 5 working days after the emergency occurred. Except in such an emergency, prior approval by the sponsor is required for changes in or deviations from a plan, and if these changes or deviations may affect the scientific soundness of the plan or the rights, safety, or welfare of human subjects, FDA and IRB in accordance with § 812.35(a) also is required.

(5) *Informed consent.* If an investigator uses a device without obtaining informed consent, the investigator shall report such use to the sponsor and the reviewing IRB within 5 working days after the use occurs.

(6) *Final report.* An investigator shall, within 3 months after termination or completion of the investigation or the investigator's part of the investigation, submit a final report to the sponsor and the reviewing IRB.

(7) *Other.* An investigator shall, upon request by a reviewing IRB or FDA, provide accurate, complete, and current information about any aspect of the investigation.

(b) *Sponsor reports.* A sponsor shall prepare and submit the following complete, accurate, and timely reports:

(1) *Unanticipated adverse device effects.* A sponsor who conducts an evaluation of an unanticipated adverse device effect under § 812.46(b) shall report the results of such evaluation to FDA and to all reviewing IRB's and participating investigators within 10 working days after the sponsor first receives notice of the effect. Thereafter the sponsor shall submit such additional reports concerning the effect as FDA requests.

(2) *Withdrawal of IRB approval.* A sponsor shall notify FDA and all reviewing IRB's and participating investigators of any withdrawal of approval of an investigation or a part of an investigation by a reviewing IRB within 5 working days after receipt of the withdrawal of approval.

(3) *Withdrawal of FDA approval.* A sponsor shall notify all reviewing IRB's and participating investigators of any withdrawal of FDA approval of the investigation, and shall do so within 5 working days after receipt of notice of the withdrawal of approval.

(4) *Current investigator list.* A sponsor shall submit to FDA, at 6-month intervals, a current list of the names and addresses of all investigators participating in the investigation. The sponsor shall submit the first such list 6 months after FDA approval.

(5) *Progress reports.* At regular intervals, and at least yearly, a sponsor shall submit progress reports to all reviewing IRB's. In the case of a significant risk device, the sponsor shall also submit progress reports to FDA.

(6) *Recall and device disposition.* A sponsor shall notify FDA and all reviewing IRB's of any request that an investigator return, repair, or otherwise dispose of any units of a device. Such notice shall occur within 30 working days after the request is made and shall state why the request was made.

(7) *Final report.* In the case of a significant risk device, the sponsor shall notify FDA within 30 working days of the completion or termination of the investigation and shall submit a final report to FDA and all reviewing the IRB's and participating investigators within 6 months after completion or termination. In the case of a device that is not a significant risk device, the sponsor shall submit a final report to all reviewing IRB's within 6 months after termination or completion.

(8) *Informed consent.* A sponsor shall submit to FDA a copy of any report by an investigator under paragraph (a)(5) of this section of use of a device without obtaining informed consent, within 5 working days of receipt of notice of such use.

(9) *Significant risk device determinations.* If an IRB determines that a device is a significant risk device, and the sponsor had proposed that the IRB consider the device not to be a significant risk device, the sponsor

shall submit to FDA a report of the IRB's determination within 5 working days after the sponsor first learns of the IRB's determination.

(10) *Other.* A sponsor shall, upon request by a reviewing IRB or FDA, provide accurate, complete, and current information about any aspect of the investigation.

(Secs. 406, 408, 409, 502, 503, 505, 506, 507, 510, 513-516, 518-520, 701(a), 706, and 801, 52 Stat. 1049-1053 as amended, 1055, 1058 as amended, 55 Stat 851 as amended, 59 Stat. 463 as amended, 68 Stat. 511-517 as amended, 72 Stat. 1785-1788 as amended, 74 Stat. 399-407 as amended, 76 Stat. 794-795 as amended, 90 Stat. 540-560, 562-574 (21 U.S.C. 346, 346a, 348, 352, 353, 355, 356, 357, 360, 360c-360f, 360h-360j, 371(a), 376 and 381); secs. 215, 301, 351, 354-360F, 58 Stat. 690, 702 as amended, 82 Stat. 1173-1186 as amended (42 U.S.C. 216, 241, 262, 263b-263n))

[45 FR 3751, Jan. 18, 1980, as amended at 45 FR 58843, Sept. 5, 1980; 48 FR 15622, Apr. 12, 1983]

PART 813—INVESTIGATIONAL EXEMPTIONS FOR INTRAOCULAR LENSES

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AUTHORITY: Secs. 301, 501, 502, 520, 701, 704, 801, 52 Stat. 1042-1043 as amended, 1049-1051 as amended, 1055, 90 Stat. 567, 569-571, 576-578 (21 U.S.C. 331, 351, 352, 360j, 371, 374, 381).

SOURCE: 42 FR 58889, Nov. 11, 1977, unless otherwise noted.

Subpart A—General Provisions

§ 813.1 Scope.

(a) *General.* This part provides that intraocular lenses may be exempted from any of the requirements of the act enumerated in paragraph (b) of this section that would otherwise be applicable to the device, to permit investigational studies of the device by experts who are qualified by scientific training and experience to investigate the safety and effectiveness of the lenses. This part implements sections 520(g) and 520(l) of the act with respect to intraocular lenses.

(b) *Effect of exemption.* (1) In general, intraocular lenses are exempted from provisions of the following sections of the act and regulations thereunder when an application for exemption applicable to the lenses is in effect under this part: Misbranding under section 502, registration and premarket notification under section 510, performance standards under section 514, premarket approval under section 515, records and reports under section 519, restricted devices under section 520(e), good manufacturing practices under section 520(f), and color additives under section 706.

(2) Intraocular lenses shall not be exempted from a provision of the act listed in paragraph (b)(1) of this section where the Commissioner indicates that the lens is not exempt from such a provision in an order of disapproval, approval, or approval with modifications under § 813.30.

§ 813.2 Applicability.

This part applies to all implantations of intraocular lenses in humans unless a premarket approval application has been approved for these lenses under section 515 of the act.

§ 813.3 Definitions.

(a) "Intraocular lens" means a lens intended to replace surgically the natural lens of the human eye. An intraocular lens is, for purposes of this part, synonymous with "investigational device," lens, or lenses.

(b) "Investigational device" means a device that is used in an investigational study involving human subjects, where the study is for the purpose of determining if the device is safe or effective.

(c) "Investigational plan" means a plan or protocol for using an investigational device in an investigational study. See § 813.25 for requirements applicable to an investigational plan.

(d) "Investigational study" means a study involving human subjects when the study is for the purpose of determining if an investigational device is safe or effective and includes any implantation in a human of an intraocular lens for which there is no approved application for premarket approval under section 515 of the act.

(e) "Investigator" means an individual who actually conducts an investigational study, i.e., under whose immediate direction the investigational device is administered or dispensed to, or used involving, a subject.

(f) "Monitor," when used as a noun, means an individual selected by a sponsor or contract research organization to oversee the progress of an investigational study. The monitor may be a full-time employee of a sponsor or contract research organization or a consultant to the sponsor or contract research organization. ("Monitor," when used as a verb, means the act of reviewing the progress of an investigational study.)

(g) "Sponsor" means a person who initiates an investigational study, but who does not actually conduct the study (i.e., the investigational device is administered or dispensed to, or used involving, a subject under the immediate direction of another individual). A person other than an individual, e.g., corporation or government agency, that uses one or more of its own employees to conduct an investigational study that it has initiated is considered to be a sponsor (not a sponsor-investigator), and the employees are considered to be investigators.

(h) "Sponsor-investigator" means an individual who both initiates and actually conducts, alone or with others, an investigational study (i.e., under whose immediate direction the investigational device is administered or dispensed to, or used involving, a subject). The term does not include any person other than an individual. Any sponsor-investigator shall carry out the responsibilites under this part of a sponsor and of an investigator.

(i) "Institution" means a person (other than an individual) who engages in the conduct of research on human subjects or in the delivery of medical services to human subjects as a primary activity or as an adjunct to providing residential or custodial care to human beings. The term includes a hospital, retirement home, prison, university, or device manufacturer. Facility as used in section 520(g) of the act is deemed to by synonymous with the term institution for purposes of this part.

(j) "Subject" means an individual who is or becomes a paticipant in an investigational study, either as a recipient of the investigational device or as a control. A subject may be either a nonpatient volunteer or a patient on whom the intraocular lens might have a therapeutic effect.

(k) "Person" includes an individual, partnership, corporation, association, scientific establishment, government agency, and any other legal entity.

(l) "Institutional review committee" means a committee (appointed by an institution to review and monitor investigations in which human subjects participate) whose major responsibility is the protection of human subjects from risk to their health, safety, or dignity in accordance with the current professional standards and the requirements of this part. Such a committee may be known as an institutional review board or by other names.

§ 813.5 General qualifications for an exemption.

A shipment of an intraocular lens is exempt from any or all the otherwise applicable requirements of the act enumerated in § 813.1(b)(1) if all the following conditions are met:

(a) The label of the device bears the following: the name and place of business of the manufacturer, packer, or distributor in accordance with § 801.1 of this chapter; the quantity of contents; the sterility shelf life of the lens; and the statement, "Caution—investigational device. Limited by Federal (or United States) law to investigational use".

(b) The labeling of the intraocular lens is not false or misleading in any particular.

(c) (1) An application for investigational device exemption covering that shipment was submitted by the sponsor under Subpart B of this part, and the requisite time has elapsed following the date of receipt of the application by the Food and Drug Administration to permit the investigational study to begin under § 813.30(b).

(2) The Commissioner has not disapproved the application or withdrawn the exemption.

(3) Each shipment of the intraocular lens is made in accordance with the commitments in the application and any conditions imposed in the Commissioner's approval of the application.

(4) The sponsor has complied with the requirements of Subparts B, C, and G of this part, any institutional review committee that is to review and approve the investigational study for which shipment is made has complied with the requirements of Subparts D and G of this part, and the investigator(s) to which the shipment is to be made has complied with the requirements of Subparts E and G of this part and with the requirements for informed consent contained in Part 50 of this chapter.

(d) If the shipment is to be imported into or exported from the United States, the requirements of § 813.19 have been met.

(Secs. 520 (g) and (l), 701(a), 52 Stat. 1055, 90 Stat. 569-571, 572-574 (21 U.S.C. 360j (g) and (l), 371(a)))

[42 FR 58889, Nov. 11, 1977, as amended at 47 FR 46079, Oct. 15, 1982]

§ 813.10 Petitions for waiver of requirements.

(a) Any person subject to any requirement under this part may petition the Commissioner for a waiver of such requirement. Such a petition shall be submitted in accordance with § 10.30 of this chapter and shall set forth the basis for the petitioner's belief that compliance with the requirement is not necessary to achieve the objectives of this part and, where appropriate, any alternative means to achieve the objective of the requirement from which the waiver is sought.

(b) The Commissioner may, at his discretion, grant a petition for a waiver submitted under this section if he finds that compliance with the requirement from which the waiver is sought is not necessary to achieve the objectives of this part and, where appropriate, that the proposed alternative means will achieve the objective of the requirement from which the waiver is sought.

(c) The person who submits a petition under this section continues to be subject to the requirement from which the waiver is sought unless and until the Commissioner grants the petition.

§ 813.12 Information previously submitted.

Wherever this part requires the submission to the Food and Drug Administration of information or data that previously had been submitted in accordance with this part or other parts of this chapter, the information or data need not be resubmitted but may be incorporated by reference.

§ 813.19 Requirements applicable to importers and exporters of intraocular lenses.

(a) Any person who imports or offers for importation into the United States an intraocular lens shall assure that all the following requirements are met:

(1) The labeling of such lens complies with § 813.5 (a) and (b).

(2) The importer of such shipment is an agent in the United States of the foreign exporter or is the ultimate consignee, and the foreign exporter or the ultimate consignee has, prior to such shipment, completed and submitted to the Food and Drug Administration an application for an investigational device exemption in accordance with § 813.20 and acts as the sponsor of the investigational study to assure compliance with the procedures, conditions, and requirements of this part.

(3) The requisite time has elapsed after the date of receipt of the application by the Food and Drug Administration to permit the investigational study to begin under § 813.30(b).

(4) The Commissioner has not disapproved the application or withdrawn the exemption.

(b) Any person who exports an intraocular lens from the United States to a foreign country shall comply with all the following requirements:

(1) The lens shall conform to the specifications of the foreign purchaser.

(2) The lens shall comply with the laws of the country to which it is being exported.

(3) The label on the outside of the shipping package shall indicate that the lens is intended for export.

(4) The lens shall not be sold or offered for sale in domestic commerce.

(5) The person shall obtain the approval of the exportation of the lens from the country to which it is intended for export.

(6) The person shall request and obtain from the Commissioner a determination that the exportation of the device is not contrary to the public health and safety and has the approval of the country to which it is intended for export.

Subpart B—Applications for Exemption for Investigational Studies Involving Human Subjects

§ 813.20 Application.

(a) The sponsor of an investigational study shall submit to the Food and Drug Administration a completed application for an investigational device exemption that has been signed by the sponsor or an authorized representative of the sponsor. Three copies of the application and any material required to accompany the application, bound and contained in volumes of reasonable size, shall be sent by registered mail or hand delivered to the Bureau of Medical Devices, Document Control Center (HFK-20), Food and Drug Administration, 8757 Georgia Ave., Silver Spring, Md. 20910. Any subsequent reports, correspondence concerning an application, and supplemental application submitted under § 813.39 also shall be submitted in triplicate by registered mail or hand delivered to this address. The outside wrapper of any application or supplemental application should include the statement "Application (or Supplemental Application) for Investigational Device Exemption" and the outside wrapper of any reports or correspondence should include the statement, "Regarding an Investigational Device Exemption".

(b) An application for an investigational device exemption for an intraocular lens shall include the following information:

(1) A brief statement of its intended use(s) and how it is to be administered.

(2) A description of all components, ingredients, and properties and a description of the principle of operation of the device and any anticipated changes in the device that may occur in the course of the study in enough detail so that a scientist or physician familiar with the general type of lens can make a knowledgeable judgment about the anticipated safety and effectiveness of the lens in the proposed investigational study.

(3) A description of those methods, facilities, and controls, used for the manufacture, processing, packing, and storage of the device in enough detail so that a person generally informed in that area can make a knowledgeable judgment about the safety and effectiveness of the device in the proposed investigational study.

(4) A statement of the location(s) of the study and whether an institutional review committee(s) is to monitor the study at such location(s).

(5) A report of prior investigations of the device that meets the requirements of § 813.27 and a summary of the investigational plan.

(6) (i) A statement from the sponsor that an investigational plan that meets the requirements of § 813.25 and a report of prior investigations of the device that meets the requirements of § 813.27 have been submitted to and approved by the institutional review committee, or (ii) if no institutional review committee exists and one cannot be formed, a statement from the head of the institution that such a committee cannot be formed, and copies of the investigational plan and the report of prior investigations.

(7) A statement from any institutional review committee (where a committee is to monitor the study), signed by the chairman, that the committee has approved the investigational plan and has reviewed the report of prior investigations of the lens, that the committee will review the study periodically at intervals appropriate to the degree of risk but not to exceed 1 year, and that it will review reports of unexpected adverse effects on a timely basis for the purpose of determining if the study should be continued.

(8) A copy of all informational materials to be given to subjects, including all form(s) to be used to obtain informed consent of human subjects as required by Part 50 of this chapter (this material may be appended to the investigational plan or the summary of the investigational plan).

(9) A copy of all informational material, including labels and other labeling, which is to be supplied to investigators as required by § 813.47(a).

(10) A description of the scientific training and experience that the sponsor considers appropriate to qualify individuals as suitable experts to investigate the safety and effectiveness of the intraocular lens. (See § 813.43(a).)

(11) A copy of the agreement signed by investigators who will be participating, to comply with Subparts E and G of this part and Part 50 of this chapter as required by § 813.43(b).

(12) The name and a summary of the training and experience of the individual who is to monitor the progress of the study for the sponsor as required by Subpart C.

(13) A statement as to whether any institutional review committee has ever disapproved any investigational study of the device and the reasons for such disapproval.

(14) A statement that the sponsor will comply with each of the requirements of Subparts C and G of this part.

(15) A statement by a sponsor notifying FDA if he intends to charge investigators and subjects for the device.

(16) A statement by the sponsor of his reasons for any request for a waiver of the requirement of § 813.30(a) that a study shall not begin before the expiration of 30 days after the Food and Drug Administration has received an application meeting the re-

quirements of this subpart, if such waiver is requested.

(17) A claim for categorical exclusion under § 25.24 of this chapter or an environmental assessment under § 25.31 of this chapter.

(18) Any other information relevant to review of the application required by the Food and Drug Administration to be submitted. The sponsor may refuse to provide the information requested under paragraph (b)(18) of this section and treat FDA's request as a final disapproval for purposes of requesting a regulatory hearing under § 813.30. If a sponsor fails to respond to a request for information within the time prescribed in a request, FDA may treat the application as withdrawn.

(Secs. 520 (g) and (l), 701(a), 52 Stat. 1055, 90 Stat. 569-571, 572-574 (21 U.S.C. 360j (g) and (l), 371(a)))

[42 FR 58889, Nov. 11, 1977, as amended at 47 FR 46079, Oct. 15, 1982; 50 FR 16669, Apr. 26, 1985]

§ 813.25 Investigational plan.

(a) The investigational plan for the investigational study of an intraocular lens shall include the following:

(1) A statement of the intended use of the lens;

(2) A general outline of the plan and any anticipated or forseeable changes or variations in the plan that may be made based on experience gained in the study;

(3) A description of what results are expected from the investigational study;

(4) A justification for beginning the study, taking into account prior experience with the intraocular lens;

(5) the expected duration of the investigational study;

(6) Identification of the investigator or investigators, the facilities where the study will occur, and any institutional review committees that will supervise the study;

(7) The patient population in which the lens will be used (in terms of age, sex, and condition) and the size of each population;

(8) A justification for using such patient population and of the size of each population;

(9) The sponsor's plan for monitoring the study in accordance with § 813.46;

(10) A description of records to be maintained, and the reports to be made, by the investigator(s) and the sponsor to assure compliance with the plan and enable the progress of the investigation and the safety and effectiveness of the lenses to be reviewed by the sponsor, any institutional review committee, and the Food and Drug Administration;

(11) The plan for obtaining informed consent from subjects and copies of all informational materials to be given to subjects, including all forms and materials to be used in obtaining such consent; and

(12) A description of the scientific training and experience the sponsor considers appropriate to qualify individuals as suitable experts to investigate the safety and effectiveness of the intraocular lens. (See § 813.43(a)).

(b) The procedures and conditions in the investigational plan may vary depending on the following:

(1) The scope and duration of the investigational study;

(2) The number of human subjects who are to be involved in the study;

(3) The need to permit changes to be made in the device during the study conducted in accordance with the plan; and

(4) The purpose of the study, e.g., whether the study is designed for developing data to obtain approval for the commercial distribution of the device.

(c) When an investigational study is to develop data to obtain approval for commercial distribution of the device, the Food and Drug Administration will not ordinarily regard an investigational plan as capable of providing data that will support an application for such approval unless it provides for more than one independent qualified investigator.

(d) The investigational plan may provide for additional animal tests to be made during the investigational study.

[42 FR 58889, Nov. 11, 1977; 43 FR 1940, Jan. 13, 1978]

§ 813.27 Report of prior experience with the lens.

(a) A report of prior investigations with the lens shall be submitted to an institutional review committee and to the Food and Drug Administration.

(b) The report of prior investigations of a lens shall include:

(1) A bibliography of any publications relevant to the investigational study and copies of significant publications both adverse and supporting.

(2) Any other unpublished information available to the sponsor, both adverse and supporting, information relating to preclinical investigations of the lens, including appropriate tests in animals and tests in vitro, and prior clinical investigations of the device or clinical experience with the device from commercial marketing, whether in the United States or in foreign countries, in sufficient detail so that a scientist or physician familiar with the general type of lens can make a knowledgeable judgment about the anticipated safety and effectiveness of the device in the proposed investigational study.

(c) Prior investigations of a lens shall not be considered adequate to justify an investigational study involving human subjects unless the conditions of the prior investigations of the lens are comparable to the conditions of the proposed investigational study.

§ 813.30 Food and Drug Administration review of and action on an application.

(a) Upon receipt of an application for an investigational device exemption submitted in accordance with this subpart, the Food and Drug Administration will notify the sponsor of the date of such receipt and inform the sponsor that the investigational study may not be begun until 30 days after the date of the agency's receipt of the application, unless the agency has decided to waive the 30-day time requirement and so informs the sponsor.

(b) An application for an investigational device exemption shall be deemed to be approved on the 30th day after the Food and Drug Administration received the application unless, on or before such day, the Commissioner finds that the application does not meet the requirements of this part and by order disapproves the application, stating his reasons therefor, or finds the application deficient and requests additional information or suggests revisions, or approves the application with modifications. If the Commissioner requests additional information or suggests revisions, the sponsor may treat the application as disapproved for purposes of requesting a regulatory hearing under Part 16 of this chapter.

(c) The Commissioner may by order disapprove an application if he makes any of the following findings:

(1) The application contains an untrue statement of a material fact or omits material information required by § 813.20.

(2) The report of prior investigations of the intraocular lens is inadequate to support a conclusion that it is reasonably safe to begin or continue the proposed investigational study.

(3) There is reason to believe that the lens may be unsafe or ineffective when used for the purpose or in the manner for which it is to be investigated.

(4) The investigational plan described in the application is not a reasonable plan, in whole or in part, for a scientific investigation to determine whether the investigational device is safe or effective.

(5) The methods, facilities, and controls used for the manufacturing, processing, packing, storage, or implantation of the lens do not assure adequately the safety and effectiveness of the lens.

(6) The sponsor's proposed use of the lens is not intended solely for an investigational study, since it is being or is to be sold or otherwise commercially distributed in a manner not justified by the requirements of the investigational study and not permitted by this part.

(7) The proposed investigational study on which the application is submitted does not conform to procedures, conditions, or requirements prescribed in this part.

(8) The proposed investigational study subjects human subjects to undue risks. In assessing risks, the Commissioner shall consider, among

other things, the factors prescribed in § 813.66(f).

(d) The Commissioner shall notify the sponsor of an approval, disapproval, or approval with modifications of an application. The notification shall contain the order of the approval, disapproval, or approval with modifications and a complete statement of the reasons for the order. An order that is a notification of disapproval or approval with modifications shall advise the sponsor that he has recourse to an opportunity for a regulatory hearing pursuant to Part 16 of this chapter.

(e) The Commissioner may in his discretion decide not to disapprove an application for which there are grounds for disapproval if he concludes that risks do not outweigh the benefits to subjects.

§ 813.35 Withdrawal of an exemption.

(a) The Commissioner may by order withdraw an exemption granted under this part if he makes any of the following findings:

(1) The application for such exemption or any subsequent report contains an untrue statement of material fact or omits material information required by §§ 813.20, 813.39, or Subpart C of this part.

(2) The report of prior investigations of the device is inadequate to support a conclusion that it is reasonably safe to continue the investigational study involving human subjects.

(3) There is reason to believe that the investigational device may be unsafe or ineffective when used for the purposes or in the manner for which it is investigated.

(4) The investigational plan described in the application is not a reasonable plan, in whole or in part, for a scientific investigation to determine whether the investigational device is safe or effective.

(5) The methods, facilities, and controls used for the manufacturing, processing, packing, storage, or installation of the investigational device do not adequately assure its safety and effectiveness.

(6) The investigational study is not being conducted in accordance with the investigational plan submitted to the Food and Drug Administration or the institutional review committee; or any change in, or deviation from, the investigational plan was not approved as required by § 813.39 and § 813.105.

(7) The sponsor's use of the investigational device is not solely for an investigational study since it is being or is to be sold or otherwise commercially distributed in a manner not justified by the requirements of the investigational study and not permitted by this part.

(8) The sponsor has failed to submit an application for premarket approval of the device when requested to do so by the Food and Drug Administration pursuant to § 813.46(d).

(9) The investigational study does not conform to procedures, conditions, or requirements prescribed under this part.

(10) The investigational study subjects human subjects to undue risks. In assessing risks, the Commissioner shall consider, among other things, the factors prescribed in § 813.66(f).

(11) The process of review or monitoring undertaken by the institutional review committee that is monitoring the study is inadequate.

(b) The Commissioner may in his discretion decide not to disapprove an application for which there are grounds for disapproval if he concludes that the risks do not outweigh the benefits to subjects.

(c) An order under this section shall include a complete statement of the reasons for the Commissioner's action. Such order shall be issued only after the sponsor has been afforded an opportunity for a regulatory hearing pursuant to Part 16 of the chapter, except that the order may be issued before providing an opportunity for such hearing if the Commissioner determines that the continuation of testing under the exemption with respect to which the order is to be issued will result in an unreasonable risk to the public health or safety.

(d) An exemption that has been withdrawn under section may be reinstated if the sponsor satisfies the Commissioner that the grounds for withdrawal no longer apply.

[42 FR 58889, Nov. 11, 1977; 43 FR 1940, Jan. 13, 1978]

§ 813.38 Confidentiality of data and information in an application.

(a) The existence of an application for an investigational device exemption will not be disclosed by the Food and Drug Administration unless it has previously been publicly disclosed or acknowledged.

(b) The availability for public dislosure of all data and information in the Food and Drug Administration file concerning the application shall be handled in accordance with the provisions established in § 314.14 of this chapter for the confidentiality of data and information in new drug applications.

(c) Notwithstanding the provisions of § 314.14 of this chapter, the Food and Drug Administration shall disclose upon request to an individual in whom an intraocular lens has been used a copy of any adverse reaction report relating to such use.

§ 813.39 Supplemental applications and submissions concerning applications.

(a) Except as provided in paragraphs (b), (c), and (d) of this section, information contained in an application submitted under § 813.20 may be updated by means of a report to the Food and Drug Administration under § 813.153.

(b) (1) Whenever the sponsor or any investigator participating in an investigational study wishes to implement a change in, or deviation from, the investigational plan submitted to the Food and Drug Administration under § 813.20 that may affect the validity of the study or the rights or safety of the human subjects under the criteria in paragraph (b)(3) of this section, the sponsor shall submit to the Food and Drug Administration a supplemental application describing the proposed change or deviation and the justification therefor. Except as provided in paragraph (b)(2) of this section, the sponsor shall submit the supplemental application before the change or deviation is implemented, shall obtain the prior review and approval of any institutional review committee pursuant to §§ 813.42(d) and 813.105, shall attach to such supplemental application a copy of the approval of such change or deviation by such committee, and shall not permit the change or deviation to be implemented unless and until the supplemental application is approved or deemed approved under § 813.30(b), except as described in paragraph (b)(2) of this section.

(2) When a change or deviation is necessary to eliminate or reduce an apparent immediate hazard to the safety of a human subject who is already participating in the investigational study, the sponsor is not required to comply with the prior approval requirements of paragraph (b)(1) of this section. The sponsor shall instead notify the Food and Drug Administration and any institutional review committee not notified by the investigator of the change or deviation and the justification therefor as soon as possible but in no event later than 5 days after he learns of such change or deviation.

(3) The following changes in, or deviations from, an investigational plan illustrate some of the situations in which prior review and approval are required under paragraph (a) of this section:

(i) A significant change in the method of administration or use of the lens.

(ii) A significant change in the number of subjects participating in the study at one time or cumulatively.

(iii) The use of subjects with medical conditions unrelated to, but possibly affecting, the scope or validity of the study.

(iv) The use of human subjects who require special consideration or protection and who are not listed specifically in the plan, e.g., children, mentally disabled individuals, or prisioners.

(v) The administration of concomitant or concurrent therapy where it is likely that an interaction with the lens might occur.

(c) The sponsor shall submit to the Food and Drug Administration the signed statements required under § 813.43(b) for any additional investigators and, as required by § 813.42(d), the statement signed by the chairman of any institutional review committee that is added to an investigational study after submission of an application for an investigational device exemption under § 813.20 (b). Any such additional statement shall be submitted before an investigator may begin participation in the investigational study.

(d) The sponsor shall submit to the Food and Drug Administration any additional informational materials to be given to subjects, including forms, or revisions in informational materials or forms, to be used by investigators to obtain informed consent of human subjects and any additional informational materials, or revision in such informational materials, supplied to investigators, which had not been submitted in an application under § 813.20(b) (8) and (9) or any subsequent reports to the Food and Drug Administration. The sponsor shall submit such forms or materials to the Food and Drug Administration at the same time that they are provided to investigators.

[42 FR 58893, Nov. 11, 1977; 43 FR 1940, Jan. 13, 1978]

Subpart C—Sponsor Responsibilities in Investigational Studies of Intraocular Lenses

§ 813.40 General.

The requirements of this subpart are applicable to sponsors of investigational studies, including sponsor-investigators.

§ 813.42 Review of the investigational study by the Food and Drug Administration and the institutional review committee.

(a) The sponsor shall submit for review and approval by the Food and Drug Administration an application for an investigational device exemption in accordance with Subpart B of this part before any human subjects are allowed to participate in the investigational study.

(b) The sponsor shall not permit any human subjects to participate in the study until the study has been approved by an institutional review committee and the application for exemption is approved by the Food and Drug Administration.

(c) The sponsor shall assure that the institutional review committee and the Food and Drug Administration are provided all the information on the proposed investigational study and the lens that they will need to review, approve, and monitor the study.

(d) The sponsor shall obtain from the institutional review committee a statement, signed by the chairman, that the committee has approved the investigational plan and has reviewed the report of prior investigations of the lens and that the committee will monitor the investigation in accordance with Subpart D of this part.

(e) The sponsor shall not implement a change in or deviate from the investigational plan, or permit a change or deviation to be implemented, unless there has been compliance with the requirements of §§ 813.39 and 813.105.

§ 813.43 Selection of investigators.

(a) The sponsor shall select as investigators only individuals who, because of their training or experience, qualify as suitable experts to investigate the safety and effectiveness of the lens. As a minimum, investigators shall have completed successfully a residency in opthalmology or its documented equivalent and be licensed to practice medicine in the State or country in which the investigational study is to take place. Sponsors shall adopt appropriate additional criteria for investigators (bearing in mind the investigational plan, the report of prior investigations of the lens, and what is known about the lens).

(b) The sponsor shall obtain from each investigator who will participate in the investigational study a signed agreement for submission to the Food and Drug Administration that includes the following:

(1) A statement of the investigator's education and experience in sufficient detail to allow determination of the investigator's qualifications for investigating the lens. Such statement shall include specific experience with the intraocular lens to be investigated, including date, amount and description of experience, and the name of the institutions where the lens was investigated or used.

(2) An agreement to comply with the investigational plan and the requirements of Subparts E and G of this part and Part 50 of this chapter.

(3) An agreement that any use of the lens involving human subjects will be under the investigator's supervision or under the supervision of another investigator who is responsible to him and who is named by the investigator in a signed statement under paragraph (b) (5) of this section.

(4) A statement as to whether any investigational study or other research by such investigator has been discontinued on the order of a sponsor, an institutional review committee, or the Food and Drug Administration.

(5) The name of any other investigator who will particpate in the investigator's supervision and responsible to him, with a statement of such other investigator's education and experience in accordance with paragraph (b)(1) of this section.

(Secs. 520 (g) and (l), 701(a), 52 Stat. 1055, 90 Stat. 569-571, 572-574 (21 U.S.C. 360j (g) and (l), 371(a)))

[42 FR 58889, Nov. 11, 1977, as amended at 47 FR 46079, Oct. 15, 1982]

§ 813.45 Control over the intraocular lens.

(a) The sponsor shall permit the lens to be shipped only to investigators who have signed statements under § 813.43 (b).

(b) If the study is suspended, terminated, completed, discontinued, or the exemption is withdrawn, the sponsor shall require the investigator to dispose of the lens in accordance with the requirements of § 813.107(b).

(c) The sponsor shall assure that the methods, facilities, and controls selected for investigating and implanting the lens are adequate to assure the device will be tested under conditions that adequately assure the safety and effectiveness of the lens in the investigational study and, where the sponsor is a manufacturer, distributor, or importer of the lens, he shall also assure that the methods, facilities, and controls used for the manufacture, processing, and storage of the lens adequately assure the safety and effectiveness of the lens in the investigational study.

§ 813.46 Monitoring the investigational study.

(a) The sponsor shall designate one or more appropriately trained and qualified individuals to monitor the progress of the investigational study on a continuing basis and evaluate the date concerning the safety and effectiveness of the lens on behalf of the sponsor upon receipt of such data from investigators, and shall assure that such monitoring and evaluation occur.

(b) The sponsor shall review the investigational study periodically at intervals appropriate to the degree of risk to assure that the requirements of this part are met.

(c) Upon discovery by the sponsor that the investigator has not complied with the requirements of this subpart and Subpart G of this part or his agreement under § 813.43(b), the sponsor shall secure the investigator's compliance or discontinue shipments to the investigator and may require the investigator to return or otherwise make appropriate disposition of the lens in accordance with the requirements of § 813.107(b), and may suspend or terminate any study being performed by the investigator for the sponsor.

(d) A sponsor shall not unduly prolong an investigational study. Where data are developed in the study that would support submission of an application for premarket approval of the lens pursuant to section 515 of the act, the sponsor shall either submit such an application or discontinue the study.

(e) Where the sponsor learns from an investigation and report of an adverse reaction under § 813.153(b) that a serious adverse reaction is lens related and presents unreasonable risk to subject involved in the study he shall discontinue the study as soon as possible but in no event later than 5 days after sufficient information is available to warrant suspension. For purposes of this section, suspension of the investigational study means that no new subjects may be added to the study. Where the Food and Drug Administration regards an adverse reaction as lens related and as presenting unreasonable risk to subjects, the agency may request or order the sponsor to supend the study and to take appropriate action to protect subjects in whom lenses have been implanted.

The sponsor shall suspend the study and take such other action as soon as possible but in no event later than 5 days after such request or order. Once the study has been suspended, the sponsor shall not resume the study without the concurrence of the Food and Drug Administration.

§ 813.47 Submitting information to investigators.

(a) The sponsor shall supply all investigators with copies of the investigational plan required under § 813.25, the report of prior investigations of the lens required under § 813.27, and labeling (including labels) for the lens that describes all relevant hazards, contraindications, adverse reactions, interfering substances, precautions suggested by prior investigations, the sterility shelf life of the lens, and experience with the lens. The labeling shall nor represent that the safety or effectiveness of the lens has been established for the purposes to be investigated.

(b) The sponsor shall notify each investigator of the completion or discontinuance of the investigational study or the withdrawal of the exemption as soon as possible but in no event later than 5 days after such action.

(c) The sponsor shall notify each investigator if an application for premarket approval of the device under section 515 of the act is approved.

§ 813.50 Promotion and sale of intraocular lenses.

(a) Neither the sponsor nor any person acting for or on behalf of the sponsor shall disseminate any promotional material representing that the lens being investigated is safe and effective for the purposes for which it is under investigation. This requirement does not restrict the full exchange of scientific information concerning the device, including dissemination of scientific findings. However, this requirement prohibits promotional claims by the sponsor that the lens is safe and effective while the device is being investigated to establish its safety and effectiveness.

(b) The sponsor of the study of an intraocular lens may distribute the lens only if the sponsor has an effective exemption under this part for all lenses sold, and all patients who receive a lens are included in an investigational study under an exemption.

Subpart D—Institutional Review Committee

§ 813.60 Requirement of institutional review committee.

An institutional review committee shall review and monitor all investigational studies of an intraocular lens, except that where an institutional review committee does not exist and one cannot be established, the sponsor of the study shall submit the investigational plan and report of prior investigations pursuant to § 813.20(b) (5) and (6) for review by the Food and Drug Administration. The Food and Drug Administration may disapprove a study that is not to be reviewed and monitored by an institutional review committee if, in the opinion of the Commissioner, the lack of institutional review committee review may expose human subjects to undue risk.

§ 813.62 Membership of an institutional review committee.

(a) Any institutional review committee that undertakes to participate in the review of a proposed study shall possess the professional competence necessary to review the specific study. An institutional review committee shall be composed of not less than five individuals with varying backgrounds to assure complete and adequate review of the investigational study. Such committee shall include, in addition to persons possessing the professional competence necessary to review scientific activities, persons whose primary concerns are in nonscientific areas, e.g., lawyers, clergymen, ethicists, social scientists, or other lay persons. No such committee shall consist entirely of members of a single professional group.

(b) The records of a committee shall identify each member by name, earned degrees, positions or occupation, representative capacity, and other pertinent indications of experience, such as board certification or licenses, sufficient to describe each member's chief anticipated contributions to such committee's deliberations. The employment or other relationship between each member and the institution and any investigator or sponsor of any investigational study reviewed and monitored by the committee shall be described in the records of the committee, e.g., full-time employee, part-time employee, member of governing panel or board, paid consultant, or unpaid consultant.

(c) No committee shall consist entirely of persons who are officers, employees, or agents of, or are otherwise associated with, the institution, apart from their membership on the committee.

(d) No member of a committee shall participate in the committee's review of monitoring of an investigational study in which he has a conflicting interest. No investigator or sponsor shall participate in the selection of members for a committee that will review his investigational study.

(e) The committee is responsible for determining whether a member has a conflict of interest and, if so, such member shall not participate in the review or monitoring of the study.

(f) An institutional review committee may in its discretion invite persons with competence in particular areas (consultants) to assist in the review of complex issues whose resolution requires expertise beyond or in addition to that available within the committee. Consultants may not vote.

§ 813.65 Procedures for review and monitoring of investigational studies by an institutional review committee.

(a) An institutional review committee shall follow written procedures adopted by either the committee or the institution for conducting its review and monitoring of investigational studies and for reporting its findings to the institution, the sponsor, and the investigator.

(b) A committee shall conduct business by a quorum, which shall be defined by written procedures. In no event shall a quorum be less than a majority of the members of the committee.

(c) A committee participating in the review of an investigational study shall monitor that study until the investigation is completed or discontinued by the sponsor or terminated or suspended by the committee or an exemption is withdrawn by the Food and Drug Administration.

§ 813.66 Procedures and criteria for review of investigational studies by an institutional review committee.

(a) Upon receipt of the proposed investigational study, including an investigational plan and a report of prior investigations of the lens from the sponsor or investigator, a committee that is to participate in the review of the study shall perform the following functions:

(1) Determine that each investigator has sucessfully completed a residency in ophthalmology or its documented equivalent, and is licensed to practice medicine in the State or country in which the investigational study is to take place.

(2) Review the investigational plan and determine that the nature of the investigational study provides a benefit to the proposed subjects such that the risks to the subjects are justified.

(3) Assure that sufficient records will be kept so as to describe clearly the results of the study.

(4) Require the investigator to notify the institutional review committee of any unanticipated side effects or increased hazards, or any changes in the investigational study, actual or proposed, that have resulted or may result from the preliminary findings of the study that could result in modification or reversal of the initial determination to authorize beginning the study.

(5) Monitor the investigational study at intervals appropriate to the degree of risk but in no event exceeding 1 year so as to assure that the study continues to be justified during the course of the study.

(6) Assure that the rights of human subjects are properly protected, that legally effective informed consent is obtained, and that the method of obtaining consent properly informs the human subject of the significant aspects of the study in accordance with Part 50 of this chapter.

(7) Receive, process, and act on complaints relating to any study under review, e.g., from subjects, sponsor, and other members of an institution's staff.

(b) If the committee has any question regarding the proposed investigational study, the committee may request the investigator or sponsor to submit additional information concerning the proposed study.

(c) The committee shall review and approve, approve with modifications, or disapprove a proposed study as soon as possible after receipt thereof.

(d) The committee may disapprove a proposed study for any reason it considers appropriate and shall disapprove a proposed study if it makes any of the following findings:

(1) The information submitted to the committee concerning the study contains an untrue statement of a material fact or omits material information required by this part.

(2) The report of prior investigations of the lens is inadequate to support a conclusion that it is reasonably safe to begin the proposed investigational study.

(3) There is reason to believe that the lens may be unsafe or ineffective when used for the purpose or in the manner for which it is to be investigated.

(4) The investigational plan is not a reasonable plan, in whole or in part, for a scientific investigation to determine whether the lens is safe or effective.

(5) The proposed investigational study does not conform to procedures, conditions, or requirements prescibed in this part.

(6) The investigator does not possess the scientific training and experience appropriate to qualify him as a suitable expert to investigate the safety and, where appropriate, effectiveness of the lens.

(7) The available clinical laboratory facilities and medical support are inadequate to assure that the study will be conducted properly and inconformity with the plan or to assure the safety of the subjects.

(e) A committee participating in the review may suspend or terminate a study after it has begun for any of the following reasons:

(1) Any reason for which the committee shall disapprove a study under paragraph (d) or (f) of this section.

(2) The investigator has disregarded committee recommendations for patient protection or has refused to cooperate with the committee, or to provide information to the committee.

(3) Experience developed during the study, or newly discovered scientific evidence not considered at the time the study was initially approved, indicates that the risks outweigh the potential benefits to the subjects.

(4) The investigator(s) who initiated the study cannot or will not continue to perform as an investigator, and a suitably qualifed replacement is not available.

(5) There is evidence of fraud in the submission of data.

(6) The institutional support available for the study is no longer sufficient in quality or amount to assure the safe continuation of the study.

(7) There has been unethical conduct on the part of the investigator in the course of the study.

(8) Such other reasons as the committee may find appropriate.

In the event the committee terminates or suspends a study, it shall notify the sponsor and the Food and Drug Administration as expenditiously as possible, stating its reasons for the suspension, the duration of the suspension, the conditions, if any, under which the study will be permitted to continue, and its recommendations for the proper care of subjects.

(f) The committee shall disapprove a proposed study as being inadequate to justify commencement of testing involving human subjects if it determines that the proposed investigational study exposes the subjects to undue risks. In assessing risks, the committee shall consider, among other things, whether:

(1) The risks to the subject are so outweighed by the sum of the benefits to the subject and the importance of the knowledge to be gained as to warrant a decision to allow the subject to accept these risks;

(2) The rights, safety, and welfare of any such subjects will be adequately protected;

(3) A legally effective informed consent will be obtained by adequate and appropriate methods in accordance with the provisions of Part 50 of this chapter; and

(4) The conduct of the activity will be reviewed at timely intervals by the institutional review committee and the sponsor.

(g) The committee shall notify the sponsor or investigator who submitted the proposal of its decision on the proposed study. Notification of approval with modifications or of disapproval shall contain a statement of the reasons for the committee's approval with modificaions or disapproval.

(Secs. 520 (g) and (l), 701(a), 52 Stat. 1055, 90 Stat. 569-571, 572-574 (21 U.S.C. 360j (g) and (l), 371(a)))

[42 FR 58889, Nov. 11, 1977, as amended at 47 FR 46080, Oct. 15, 1982]

§ 813.70 Review by institution.

Approval, including approval with modifications, by an institutional review committee may be subject to further appropriate review and approval or rejection by institutional officials, but disapproval by the committee may not be overruled by such officials.

§ 813.79 Actions where review by an institutional review committee is inadequate.

(a) The Commissioner may determine that the process of review undertaken by an institutional review committee is inadequate if he finds that it failed to meet the requirements of this subpart or Subpart G of this part.

(b) If the commissioner finds that the process of review or monitoring undertaken by the committee is inadequate, he may:

(1) Request the committee to change it process of review or monitoring to meet the requirements of this subpart and Subpart G of this part;

(2) Require the sponsor to obtain review or monitoring by a committee whose process of review or monitoring meets such requirements;

(3) Require that the application be reviewed by the Food and Drug Administration; or

(4) Disapprove the application for an investigational device exemption or withdraw the exemption.

Subpart E—Investigator Responsibilities in Investigational Studies of Intraocular Lenses

§ 813.100 General.

The requirements of this subpart are applicable to investigators of investigational studies, including sponsor investigators.

§ 813.101 Review of investigational study by the Food and Drug Administration.

An investigator shall not allow human subjects to participate in an investigational study until such time as an investigational device exemption has been obtained from the Food and Drug Administration pursuant to Subpart B of this part.

§ 813.103 Review of investigational study by institutional review committee.

Where the investigation of an intraocular lens is subject to an institutional review requirement under § 813.60:

(a) An investigator shall not allow human subjects to participate in an investigational study until the committee has approved the study.

(b) An investigator shall not implement a change in, or deviate from, the investigational plan until he has complied with the requirements of § 813.105.

(c) An investigator shall report to the committee and to the sponsor any serious adverse reaction occurring in the study that may reasonably be regarded as lens related and that was not previously expected in nature or severity or degree of incidence in the investigational plan.

(d) An investigator shall notify the committee within 3 months after completion or discontinuance of, or the withdrawal of the exemption for, the entire investigational study or of his portion of the study, whichever occurs first.

(e) An investigator shall provide accurate and adequate information regarding the investigational study to the committee in response to its request.

§ 813.105 Conformity to investigational plan.

(a) Whenever the investigator desires to implement a change in the investigational study that will result in a deviation from the investigational plan, he shall:

(1) Where such change may reasonably be expected to increase the risks to subjects and/or affect the scientific validity of the study under the criteria in § 813.39(b), notify the sponsor of the proposed change and obtain the sponsor's assent; submit, or assure that the sponsor submits, to the investigational review committee notice of such change and obtain the written approval of the investigational review committee; and submit, or assure that the sponsor submits, to the Food and Drug Administration a supplemental application in accordance with § 813.39(b) and obtain the approval of the Food and Drug Administration before implementing the proposed change.

(2) Where such change may not reasonably be expected to increase the risks to the subjects, and does not affect the scientific validity of the study involved, the investigator may implement the change, but shall notify the sponsor and the institutional review committee involved. The notice of the change shall be reflected in sponsor, investigator, and institutional review committee records and in reports under § 813.153(c) and shall be reviewed by the institutional review committee in the regular course of business.

(b) When a change in or deviation from the investigational plan is necessary to eliminate or reduce an apparent immediate hazard to the safety of a human subject who is already participating in the investigational study, the investigator is not required to comply with the prior approval requirements of paragraph (a) of this section. The investigator shall instead notify any institutional review committee and the sponsor, who shall notify the Food and Drug Administration of the change or deviation and the justification therefor as soon as possible but in no event later than 5 days after such change or deviation is implemented as required by § 813.39(b)(2).

§ 813.107 Control over intraocular lenses.

(a) An investigator shall only permit the lens to be used for administration to, or use involving, subjects who are under his personal supervision or under the supervision of another investigator who is responsible to him and who is named by the investigator in his signed statement undertaking the obligations of an investigator under § 813.43(b). An investigator shall not supply the lens to any other person for administration to, or use involving, subjects or for any other purpose, without the prior authorization of the sponsor.

(b) An investigator shall return to the sponsor any reusable or unused supply of the lens upon direction of the sponsor, or upon suspension, termination, completion, discontinuance of, or withdrawal of the exemption for, the investigational study. The sponsor may direct or agree to alternative disposition of the lens such as destruction or use in animal or in vitro experiments.

§ 813.119 Disqualification of a clinical investigator.

(a) *Purposes.* The purpose(s) of disqualification of an investigator who has violated the regulations set forth in this part may be one or both of the following:

(1) To preclude the investigator from conducting clinical investigations subject to requirements under the act for prior submission to the Food and Drug Administration until such time as it becomes likely that he will abide by such regulations or that such violations will not recur. The determination to disqualify an investigator does not necessarily consitute a finding or recommendation that the investigator is not qualified to practice or teach medicine or should be subject to other sanctions by other persons such as licensing boards or employers.

(2) To exclude the consideration of any clinical investigations or portions

thereof in support of applications for an investigational exemption or for premarket approval from the Food and Drug Administration, which investigations have been conducted in whole or in part by the investigator, until such time as it becomes likely that he will abide by such regulations or that such violations will not recur or that it can be adequately demonstrated that such violations did not occur during or affect the validity or acceptability of a particular investigation or investigations. The determinations that a clinical investigation may not be considered in support of an application for exemption or premarket approval does not, however, relieve the applicant for such an application of any obligation under any other applicable regulation to submit the results of the investigation to the Food and Drug Administration.

(b) *Grounds for disqualification.* The Commissioner may disqualify an investigator upon finding all the following:

(1) The investigator violated any of the regulations set forth in this part;

(2) The violation or violations adversely affected the validity of the clinical investigation, the rights of the human subjects, and/or the safety of the subjects; and

(3) Other lesser regulatory actions, e.g., warnings or rejection of data from individual investigations, have not been or will probably not be adequate to assure that the investigator will comply with such regulations in the future.

(c) *Notice of and opportunity for a hearing on proposed disqualification.* (1) Whenever the commissioner has information indicating that grounds exist under paragraph (b) of this section that in his opinion may justify disqualification of an investigator, he may issue to the investigator a written notice proposing that the investigator be disqualifed.

(2) A hearing on the disqualification of an investigator shall be conducted in accordance with the requirements for a regulatory hearing set forth in Part 16 of this chapter.

(d) *Final order on disqualification.* (1) If the Commissioner, after the regulatory hearing or after the time for requesting a hearing expires without a request being made, upon an evaluation of the administrative record of the disqualification proceeding, makes the findings required in paragraph (b) of this section, he shall issue a final order disqualifying the investigator. Such order shall include a statement of the basis for that determination and shall prescribe any actions (set forth in paragraph (e) of this section) to be taken with regard to on going regulated clinical investigations being conducted by the investigator. Upon issuing a final order, the commissioner shall notify (with a copy of the order) the investigator of the action, as well as the sponsor of each clinical investigation subject to requirements for prior submission to the Food and Drug Administration that was being conducted by the investigator and has not been terminated or discontinued or the exemption under which it is being conducted has not been terminated or withdrawn by the Food and Drug Administration.

(2) If the commissioner, after a regulatory hearing or after the time for requesting a hearing expires without a request being made, upon an evaluation of the administative record of the disqualification proceeding does not make the findings required in paragraph (b) of this section, he shall issue a final order terminating the disqualification proceedings. Such order shall include a statement of the basis for the that determination. Upon issuing a final order, the Commissioner shall notify the investigator and provide a copy of the order.

(e) *Actions upon disqualification.* (1) No clinical investigations subject to requirements for prior submission to the Food and Drug Administration will be authorized by the Food and Drug Administration if such investigation is to be conducted, in whole or part, by a disqualified investigator.

(2) The commissioner, after considering the nature of each ongoing clinical investigation that is being performed by the investigator and is subject to requirements for prior submission to the Food and Drug Administration, the number of subjects involved, the risks to them from suspension of the investigation, and the need for in-

volvement of an acceptable investigator, may direct, in the final order disqualifying an investigator under paragraph (c) (1) of this section, that one or more of the following actions be taken with regard to each such investigation:

(i) The investigation may be terminated or suspended in its entirety until the investigator is reinstated under paragraph (k) of this section or another investigator accepts responsiblity for the investigation.

(ii) No new subject shall be allowed to participate, or be requested to participate, in the investigation until the investigator is reinstated under paragraph (k) of this section, or another investigator accepts responsibility for the investigation.

(iii) Any human subject who has previously been allowed to participate in the investigation and who remains under the supervision of the investigator should continue to be monitored by the investigator, but the human subject shall not receive another lens until the investigator is reinstated under paragraph (k) of this section or another investigator accepts responsibility for the investigational study.

(iv) Any human subject who has been allowed to participate in the investigation and who, except for suspension of the investigation, would have received the lens shall not receive it unless another investigator accepts responsiblity for the investigation.

(f) *Disqualified investigators and applications.* Once an investigator has been disqualified, each application for an investigational exemption or for premarket approval, whether approved or not, containing or relying upon any clinical investigation performed by the investigator may be examined to determine whether the investigation was or would be essential to a regulatory decision regarding the application. If it is determined that the investigation was or would be essential, the Food and Drug Administration shall also determine whether the investigation is acceptable notwithstanding the disqualification of the investigator. Any investigation done by an investigator before or after disqualification may be presumed to be unacceptable, and the person relying on the investigation may be required to establish that the investigation was not affected by the circumstances that led to disqualification of the investigator, e.g., by submitting validating information. If the investigation is determined to be unacceptable, such investigation will be elimated from consideration in support of the application, and such elimination may serve as new information justifying the termination or withdrawal of approval of the application.

(g) *Clinical investigations begun by a disqualified investigator.* No clinical investigation begun by an investigator after the date of his disqualification will be considered in support of any application for an exemption or premarket approval application unless the investigator has been reinstated under paragraph (k) of this section. The determination that a clinical investigation may not be considered in support of an application for an exemption or premarket approval application does not, however, relieve the applicant of any obligation under any other applicable regulation to submit the results of the investigation to the Food and Drug Administration.

(h) *Public disclosure of information regarding disqualification.* (1) Upon issuance of a final order disqualifying an investigator, the Commissioner may notify any other person known to have professional relations with the investigator (e.g., other Federal government departments or agencies that support investigations possibly involving the investigator, State and local medical licensing boards and societies where the investigator practices or is licensed, and administrators and institutional or peer review boards in universities, hospitals, and other institutions in which the investigator teaches or practices) that the investigator has been disqualified by the Food and Drug Administration. Such notice may be given in the discretion of the Commissioner whenever he believes that such disclosure would further the public interest or would promote compliance with the regulations set forth in this part. Such notice, if given, shall include a copy of the final order issued under paragraph (d) of this section and shall state that the disqualification consitutues a determination by the Food and Drug Administration that the investigator is not eligible to conduct clinical investigations subject to requirements for prior submission to the Food and Drug Administration and that the results of any clinical investigations conducted by the investigator may not be considered by the Food and Drug Administration in support of any application for an exemption or premarket approval application. The notice shall further state that it is given because of the professional relations between the investigator and the person notified and that the Food and Drug Administration is not advising or recommending that any action be taken by the person notified.

(2) A determination that an investigator has been disqualified and the administrative record regarding such determination are disclosable to the public under Part 20 of this chapter.

(3) Whenever the Commissioner has reason to believe that an investigator may be subject to disqualification, he may, in his discretion, so notify the sponsor of any ongoing clinical investigation in which that investigator is participating simultaneously with or subsequent to proposing disqualification of the investigator under paragraph (c) of this section, unless there are overriding safety considerations that warrant earlier notification of the sponsor.

(i) *Alternative or additional actions to disqualification.* Disqualification of an investigator under this subpart is independent of, and neither in lieu of nor a precondition to, other proceedings or actions authorized by the act. The Food and Drug Administration may, at any time, institute any appropriate judicial proceedings (civil or criminal) and any other appropriate regulatory action in addition to or in lieu of (and prior to, simultaneously with, or subsequent to) disqualification. The Food and Drug Administration may also refer pertinent matters to another Federal, State, or local law enforcement or regulatory agency for such action as that agency deems appropriate.

(j) *Suspension or termination of an investigator by a sponsor.* The sponsor of an investigational study may at any time remove an investigator from further participation in the study, whether or not the Food and Drug Administration has begun any action to disqualify the investigator. The sponsor need not use either the grounds or the procedures for disqualification set forth in this subpart. If a sponsor removes an investigator from a study, the sponsor shall notify the Food and Drug Administration in writing of the reasons for such removal as soon as possible, but in no event later than 5 days after such removal.

(k) *Reinstatement of a disqualified investigator.* An investigator who has been disqualified may be reinstated as eligible to conduct clincial investigations subject to requirements for prior submission to the Food and Drug Administration, or as acceptable to be the source of clinical investigations to be submitted to the Food and Drug Administration, if the Commissioner determines, upon an evaluation of a written submission from the investigator, that the investigator can adequately assure that he will conduct such studies in compliance with the requirements set forth in this part. A disqualified investigator who wishes to be so reinstated shall present in writing to the Commissioner reasons why he believes he should be reinstated; the investigator shall also submit a detailed description of the corrective actions he has taken or intends to take to assure that the acts or omissions that led to disqualification will not recur. The Commissioner may condition reinstatement upon the submission of an acceptable protocol for a specific clinical investigation providing for additional corrective actions and/or the submission of special undertakings by a sponsor, an institution, an institutional review committee, or another investigator to review in detail the investigator's compliance with the requirements of this part and/or the investigator's being found in compliance with the applicable regulations upon an inspection. If an investigator is reinstated, the Commissioner shall so notify the investigator and all organizations and all persons who were notified under paragraph (h) of this section of the disqualification of the investigator. A determination that an investigator has been reinstated in disclosable to the public under Part 20 of this chapter.

Subpart F—[Reserved]

Subpart G—Inspections, Reports, and Records

§ 813.150 Inspections.

(a) Any sponsor, institutional review committee, or investigator shall permit an authorized employee of the Food and Drug Administration, at reasonable times and in a reasonable manner, to inspect and copy any records concerning the investigational study that are required to be kept by this part.

(b) Any sponsor or investigator who has authority to grant access to the facility shall also permit authorized FDA employees, at reasonable times and in a reasonable manner, to inspect any facilities where the intraocular lens is manufactured, processed, held, used, or implanted.

(c) Any investigator shall permit an authorized employee of the Food and Drug Administration to copy records that identify the names of human subjects, upon notice that the Food and Drug Administration has reason to believe that the consent of human subjects was not obtained, that reports submitted by the investigator to the sponsor or to the institutional review committee do not represent actual cases or actual results obtains, or that such reports or other required records appear to be otherwise false or misleading.

[42 FR 58889, Nov. 11, 1977; 43 FR 1940, Jan. 13, 1978]

§ 813.153 Reports.

(a) *Recall reports.* Any sponsor shall notify the Food and Drug Administration of any request that investigators return, or otherwise dispose of, any supplies of the intraocular lens, or examine any patients that previously received a lens.

(b) *Adverse reaction reports.* If during the study a seriously adverse reaction occurs that may reasonably be regarded as lens related and that was not previously expected in nature, severity, or degree of incidence in the investigational plan (including any incidence of hypopyon, intraocular infection, or acute corneal decompensation), the following actions shall be effected:

(1) The investigator shall investigate the reaction and submit an accurate and adequate report of the investigation to the sponsor and to the committee as soon as possible but in no event later than 5 days after learning of the reaction;

(2) The sponsor shall evaluate any adverse reaction report submitted by the investigator any reports received from other sources and within 5 days after learning of the adverse reaction, shall report the adverse reaction and the results of is evaluation to the Food and Drug Administration, any committee(s) monitoring the study, or part of the study, in which the reaction occurred (if the investigator(s) has not already reported the reaction to the committee(s)), and all other investigators and sponsors participating in the study. In the case of hypopyon, except where the Food and Drug Administration directs otherwise, a sponsor need only report the adverse reaction and results of his evaluation to other investigators and committees particpating in the study where the incidence of the reaction exceeds that which was previously anticipated in materials provided to investigators.

(c) *Progress reports.* (1) Any investigator shall submit accurate progress reports to the investigational review committee and sponsor (or his monitor) at appropriate intervals but in no event at intervals exceeding 1 year.

(2) The sponsor shall make accurate and adequate progress reports to the Food and Drug Administration at appropriate intervals not exceeding 1 year. Such reports shall include any significant findings of the study and any necessary amendments or corrections to previous reports or to the application to keep them accurate.

(d) *Suspension/termination reports.* (1) Any investigator shall report to the sponsor any suspension or termination of the investigational study by a committee within 5 days.

(2) Any institutional review committee shall immediately report any suspension or termination of a study it is reviewing and monitoring under this part to the Food and Drug Administration.

(e) *Final reports.* (1) Within 3 months after the completion or discontinuance of or withdrawal of the exemption for the investigational study (or the investigator's portion of the study), any investigator shall notify the committee and sponsor and make an accurate and adequate final report to the sponsor, and the final report shall include all reports not previously submitted to the sponsor but required by paragraphs (b), (c), or (d) of this section.

(2) Within 30 days after the completion or discontinuance of a study or the suspension or termination of a study by a committee, the sponsor shall notify the Food and Drug Administration of the action.

(3) Within 6 months after the study is completed, discontinued, suspended, or terminated or the exemption is withdrawn, the sponsor shall make a final report to the Food and Drug Adminstration.

§ 813.155 Records.

(a) The sponsor, any investigator, and any committee shall maintain adequate and accurate records concerning the investigational study, including copies of all correspondence, among themselves and with the Food and Drug Administration regarding the study.

(b) (1) The sponsor and any investigator shall maintain adequate and accurate records showing the shipment, receipt, or other disposition of all supplies of all lenses shipped or received.

(2) The sponsor either shall provide to each investigator an identification card that is to be provided to each subject after implantation or shall provide each subject with such a card. The card shall include the following information on each lens: Lens name, manufacturer's name and address, model number, style and serial, batch, lot, or other identification number for each lens. The sponsor and each investigator shall maintain the following records: identification by name of the investigator who received each unit of the lens and who adminstered the device; the idenfification by code of the subject who received it; and identification of each unit otherwise disposed of (including identification of the person who disposed of it, the person, if any, who received it, and the purpose or reason for its disposal, e.g., because of contamination or return to the sponsor).

(c) An institutional review committee shall prepare and maintain adequate documentation of its activities regarding each investigational study, including records of information submitted to the committee by sponsors or investigators, information compiled on committee members pursuant to § 813.62, minutes of committee meetings on issues involved in the study and their resolution, committee decisions on the study, and dated reports of successive monitoring as it is performed.

(d) Contents of investigator records. An investigator shall maintain an adequate and accurate case report on each subject, which shall include the following:

(1) All relevant observations, information, and data on the condition of the subject at the time the subject enters into the study, including information regarding any relevant previous medical history and the results of all diagnostic tests performed to determine that the subject is appropriate for entry into the study.

(2) All documentation regarding the consent of the human subjects, as required by Part 50 of this chapter.

(3) All relevant observations and data on the condition of the subject throughout the duration of his participation in the study.

(e) The sponsor shall retain a copy of any application, report, or correspondence that he submits to the Food and Drug Administration under this part.

(f) A sponsor, investigator, and institutional review committee shall maintain records required under this part for whichever of the following periods is shortest:

(1) A period of 2 years after the date on which the Food and Drug Administration approves the marketing of the lens for the purposes that were the subject of the study.

(2) A period of 5 years after the date on which the results of the study are submitted to the Food and Drug Administration in support of the marketing of the lens for the purpose that was the subject of the study.

(3) In other situations, e.g., where the investigational study does not result in the submission of an application for marketing the device for the purposes that were the subject of the study, a period of 2 years after the date on which the investigational study (not merely an investigator's portion of a study) is terminated, completed or discontinued, or the exemption is withdrawn.

(g) A Sponsor, investigator, or committee may withdraw from the responsibility for maintaining records for the period of time required in paragraph (f) of this section by transferring custody to any other person who will accept responsibility for the records. Notice of such transfer shall be given to the Food and Drug Administration.

(h) The Food and Drug Administration may require a sponsor to submit any records concerning the investigational study, including any records required to be kept under this part.

(Secs. 520 (g) and (l), 701(a), 52 Stat. 1055, 90 Stat. 569-571, 572-574 (21 U.S.C. 360j (g) and (l), 371(a)))

[42 FR 58899, Nov. 11, 1977; 43 FR 1940, Jan. 13, 1978, as amended at 47 FR 46080, Oct. 15, 1982]

Subpart H—Investigational Studies That Do Not Involve Human Subjects

§ 813.160 Conditions of exemption.

(a) Where an investigational device is intended for use in humans, a shipment of the device that is intended solely for tests in animals used only for laboratory research purposes, or for in vitro or mechanical tests or similar tests that do not involve use of human subjects, shall be exempt from any of the otherwise applicable provisions of the act listed in § 813.1(c) if:

(1) The labeling of the device complies with the requirements of § 813.5 (a) and (b) and bears the following additional statement:

CAUTION—DEVICE FOR INVESTIGATIONAL USE ONLY IN LABORATORY ANIMALS OR OTHER TESTS THAT DO NOT INVOLVE HUMAN SUBJECTS

(2) The person who ships the device under this subpart uses due diligence to assure that the consignee is regularly engaged in conducting tests in animals used only for laboratory research, or similar for in vitro or other mechanical tests or tests that do not involve use of human subjects and that the shipment of the investigational device will actually be used only in such tests.

(3) The person who ships the device under this subpart maintains adequate records showing the name and address of the consignee to whom the device is shipped, date, quantity, and batch or code mark of each shipment for a period of 2 years after such shipment and, upon the request of a properly authorized employee of the Department at reasonable times, make such records available for inspection and copying or submits such records to the Food and Drug Administration.

(b) This subpart does not apply to any use of an investigational device that involves use of human subjects.

§ 813.170 Termination of exemption.

(a) The commissioner shall terminate an exemption under this subpart if he makes either of the following findings:

(1) The person shipping an investigational device under this subpart has failed to comply with any of the conditions for the exemption under this subpart.

(2) Any of the grounds for withdrawal of an investigational device exemption under § 813.35 apply.

(b) The Commissioner shall notify the sponsor of the termination of an exemption under this subpart with a full statement of the reasons for such termination and shall afford an opportunity for a regulatory hearing under Part 16 of this chapter. The person whose exemption is terminated shall recall or otherwise assure the destruction of any unused devices.

PART 50—PROTECTION OF HUMAN SUBJECTS

Subpart A—General Provisions

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Subpart B—Informed Consent of Human Subjects

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Subpart C—Protections Pertaining to Clinical Investigations Involving Prisoners as Subjects

50.40 Applicability.
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50.44 Restrictions on clinical investigations involving prisoners.
50.46 Composition of institutional review boards where prisoners are involved.
50.48 Additional duties of the institutional review boards where prisoners are involved.

AUTHORITY: Secs. 406, 409, 502, 503, 505, 506, 507, 510, 513-516, 518-520, 701(a), 706, and 801, Pub. L. 717, 52 Stat. 1049-1054 as amended, 1055, 1058 as amended, 55 Stat. 851 as amended, 59 Stat. 463 as amended, 72 Stat. 1785-1788 as amended, 74 Stat. 399-407 as amended, 76 Stat. 794-795 as amended, 90 Stat. 540-560, 562-574 (21 U.S.C. 346, 348, 352, 353, 355, 356, 357, 360, 360c-360f, 360h-360j, 371(a), 376, and 381); secs. 215, 351, 354-360F, Pub. L. 410, 58 Stat. 690, 702 as amended, 82 Stat. 1173-1186 as amended (42 U.S.C. 216, 262, 263b-263n), unless otherwise noted.

SOURCE: 45 FR 36390, May 30, 1980, unless otherwise noted.

Subpart A—General Provisions

§ 50.1 Scope.

(a) This part applies to all clinical investigations regulated by the Food and Drug Administration under sections 505(i), 507(d), and 520(g) of the Federal Food, Drug, and Cosmetic Act, as well as clinical investigations that support applications for research or marketing permits for products regulated by the Food and Drug Administration, including food and color additives, drugs for human use, medical devices for human use, biological products for human use, and electronic products. Additional specific obligations and commitments of, and standards of conduct for, persons who sponsor or monitor clinical investigations involving particular test articles may also be found in other parts (e.g., Parts 312 and 812). Compliance with these parts is intended to protect the rights and safety of subjects involved in investigations filed with the Food and Drug Administration pursuant to sections 406, 409, 502, 503, 505, 506, 507, 510, 513-516, 518-520, 706, and 801 of the Federal Food, Drug, and Cosmetic Act and sections 351 and 354-360F of the Public Health Service Act.

(b) References in this part to regulatory sections of the Code of Federal Regulations are to Chapter I of Title 21, unless otherwise noted.

[45 FR 36390, May 30, 1980; 46 FR 8979, Jan. 27, 1981]

§ 50.3 Definitions.

As used in this part:

(a) "Act" means the Federal Food, Drug, and Cosmetic Act, as amended (secs. 201—902, 52 Stat. 1040 et seq. as amended (21 U.S.C. 321—392)).

(b) "Application for research or marketing permit" includes:

(1) A color additive petition, described in Part 71.

(2) A food additive petition, described in Parts 171 and 571.

(3) Data and information about a substance submitted as part of the procedures for establishing that the substance is generally recognized as safe for use that results or may reasonably be expected to result, directly or indirectly, in its becoming a component or otherwise affecting the characteristics of any food, described in §§ 170.30 and 570.30.

(4) Data and information about a food additive submitted as part of the procedures for food additives permitted to be used on an interim basis pending additional study, described in § 180.1.

(5) Data and information about a substance submitted as part of the procedures for establishing a tolerance for unavoidable contaminants in food and food-packaging materials, described in section 406 of the act.

(6) A "Notice of Claimed Investigational Exemption for a New Drug," described in Part 312.

(7) A new drug application, described in Part 314.

(8) Data and information about the bioavailability or bioequivalence of drugs for human use submitted as part of the procedures for issuing, amending, or repealing a bioequivalence requirement, described in Part 320.

(9) Data and information about an over-the-counter drug for human use submitted as part of the procedures for classifying these drugs as generally recognized as safe and effective and not misbranded, described in Part 330.

(10) Data and information about a prescription drug for human use submitted as part of the procedures for classifying these drugs as generally recognized as safe and effective and not misbranded, described in this chapter.

(11) Data and information about an antibiotic drug submitted as part of the procedures for issuing, amending, or repealing regulations for these drugs, described in Part 430.

(12) An application for a biological product license, described in Part 601.

(13) Data and information about a biological product submitted as part of the procedures for determining that licensed biological products are safe and effective and not misbranded, described in Part 601.

(14) Data and information about an in vitro diagnostic product submitted as part of the procedures for establishing, amending, or repealing a standard for these products, described in Part 809.

(15) An "Application for an Investigational Device Exemption," described in Part 812.

(16) Data and information about a medical device submitted as part of the procedures for classifying these devices, described in section 513.

(17) Data and information about a medical device submitted as part of the procedures for establishing, amending, or repealing a standard for these devices, described in section 514.

(18) An application for premarket approval of a medical device, described in section 515.

(19) A product development protocol for a medical device, described in section 515.

(20) Data and information about an electronic product submitted as part of the procedures for establishing, amending, or repealing a standard for these products, described in section 358 of the Public Health Service Act.

(21) Data and information about an electronic product submitted as part of the procedures for obtaining a variance from any electronic product performance standard, as described in § 1010.4.

(22) Data and information about an electronic product submitted as part of the procedures for granting, amending, or extending an exemption from a radiation safety performance standard, as described in § 1010.5.

(c) "Clinical investigation" means any experiment that involves a test article and one or more human subjects and that either is subject to requirements for prior submission to the Food and Drug Administration under section 505(i), 507(d), or 520(g) of the act, or is not subject to requirements for prior submission to the Food and Drug Administration under these sections of the act, but the results of which are intended to be submitted later to, or held for inspection by, the Food and Drug Administration as part of an application for a research or marketing permit. The term does not include experiments that are subject to the provisions of Part 58 of this chapter, regarding nonclinical laboratory studies.

(d) "Investigator" means an individual who actually conducts a clinical investigation, i.e., under whose immediate direction the test article is administered or dispensed to, or used involving, a subject, or, in the event of an investigation conducted by a team of individuals, is the responsible leader of that team.

(e) "Sponsor" means a person who initiates a clinical investigation, but who does not actually conduct the investigation, i.e., the test article is administered or dispensed to or used involving, a subject under the immediate direction of another individual. A person other than an individual (e.g., corporation or agency) that uses one or more of its own employees to conduct a clinical investigation it has initiated is considered to be a sponsor (not a sponsor-investigator), and the employees are considered to be investigators.

(f) "Sponsor-investigator" means an individual who both initiates and actually conducts, alone or with others, a clinical investigation, i.e., under whose immediate direction the test article is administered or dispensed to, or used involving, a subject. The term does not include any person other than an individual, e.g., corporation or agency.

(g) "Human subject" means an individual who is or becomes a participant in research, either as a recipient of the test article or as a control. A subject may be either a healthy human or a patient.

(h) "Institution" means any public or private entity or agency (including Federal, State, and other agencies). The word "facility" as used in section 520(g) of the act is deemed to be synonymous with the term "institution" for purposes of this part.

(i) "Institutional review board" (IRB) means any board, committee, or other group formally designated by an institution to review biomedical research involving humans as subjects, to approve the initiation of and conduct periodic review of such research. The term has the same meaning as the phrase "institutional review committee" as used in section 520(g) of the act.

(j) "Prisoner" means any individual involuntarily confined or detained in a penal institution. The term is intended to encompass individuals sentenced to such an institution under a criminal or civil statute, individuals detained in other facilities by virtue of statutes or commitment procedures that provide alternatives to criminal prosecution or incarceration in a penal institution, and individuals detained pending arraignment, trial, or sentencing.

(k) "Test article" means any drug (including a biological product for human use), medical device for human use, human food additive, color additive, electronic product, or any other article subject to regulation under the act or under sections 351 and 354-360F of the Public Health Service Act (42 U.S.C. 262 and 263b-263n).

(l) "Minimal risk" means that the risks of harm anticipated in the proposed research are not greater, considering probability and magnitude, than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests.

(m) "Legally authorized representative" means an individual or judicial or other body authorized under applicable law to consent on behalf of a prospective subject to the subject's particpation in the procedure(s) involved in the research.

(Secs. 406, 408, 409, 502, 503, 505, 506, 507, 510, 513—516, 518—520, 701(a), 706, and 801, 52 Stat. 1049—1053 as amended, 1055, 1058 as amended, 55 Stat. 851 as amended, 59 Stat. 463 as amended, 68 Stat. 511—517 as amended, 72 Stat. 1785—1788 as amended, 74 Stat. 399—407 as amended, 76 Stat. 794—795 as amended, 90 Stat. 540—560, 562—574 (21 U.S.C. 346, 346a, 348, 352, 353, 355, 356, 357, 360, 360c—360f, 360h—360j, 371(a), 376, and 381); secs. 215, 301, 351, 354—360F, 58 Stat. 690, 702 as amended, 82 Stat. 1173—1186 as amended (42 U.S.C. 216, 241, 262, 263b—263n))

[45 FR 36390, May 30, 1980, as amended at 46 FR 8950, Jan. 27, 1981]

Subpart B—Informed Consent of Human Subjects

AUTHORITY: Secs. 406, 408, 409, 502, 503, 505, 506, 507, 510, 513—516, 518—520, 701(a), 706, and 801, 52 Stat. 1049—1053 as amended, 1055, 1058 as amended, 55 Stat. 851 as amended, 59 Stat. 463 as amended, 68 Stat. 511—517 as amended, 72 Stat. 1785—1788 as amended, 74 Stat. 399—407 as amended, 76 Stat. 794—795 as amended, 90 Stat. 540—560, 562—574 (21 U.S.C. 346, 346a, 348, 352, 353, 355, 356, 357, 360, 360c—360f, 360h—360j, 371(a), 376, and 381); secs. 215, 301, 351, 354—360F, 58 Stat. 690, 702 as amended, 82 Stat. 1173—1186 as amended (42 U.S.C. 216, 241, 262, 263b—263n)).

SOURCE: 46 FR 8951, Jan. 27, 1981, unless otherwise noted.

§ 50.20 General requirements for informed consent.

Except as provided in § 50.23, no investigator may involve a human being as a subject in research covered by these regulations unless the investigator has obtained the legally effective informed consent of the subject or the subject's legally authorized representative. An investigator shall seek such consent only under circumstances that provide the prospective subject or the representative sufficient opportunity to consider whether or not to participate and that minimize the possibility of coercion or undue influence. The information that is given to the subject or the representative shall be in language understandable to the subject or the representative. No informed consent, whether oral or written, may include any exculpatory language through which the subject or the representative is made to waive or appear to waive any of the subject's legal rights, or releases or appears to release the investigator, the sponsor, the institution, or its agents from liability for negligence.

§ 50.21 Effective date.

The requirements for informed consent set out in this part apply to all human subjects entering a clinical investigation that commences on or after July 27, 1981.

§ 50.23 Exception from general requirements.

(a) The obtaining of informed consent shall be deemed feasible unless, before use of the test article (except as provided in paragraph (b) of this section), both the investigator and a physician who is not otherwise participating in the clinical investigation certify in writing all of the following:

(1) The human subject is confronted by a life-threatening situation necessitating the use of the test article.

(2) Informed consent cannot be obtained from the subject because of an

inability to communicate with, or obtain legally effective consent from, the subject.

(3) Time is not sufficient to obtain consent from the subject's legal representative.

(4) There is available no alternative method of approved or generally recognized therapy that provides an equal or greater likelihood of saving the life of the subject.

(b) If immediate use of the test article is, in the investigator's opinion, required to preserve the life of the subject, and time is not sufficient to obtain the independent determination required in paragraph (a) of this section in advance of using the test article, the determinations of the clinical investigator shall be made and, within 5 working days after the use of the article, be reviewed and evaluated in writing by a physician who is not participating in the clinical investigation.

(c) The documentation required in paragraph (a) or (b) of this section shall be submitted to the IRB within 5 working days after the use of the test article.

§ 50.25 Elements of informed consent.

(a) *Basic elements of informed consent.* In seeking informed consent, the following information shall be provided to each subject:

(1) A statement that the study involves research, an explanation of the purposes of the research and the expected duration of the subject's participation, a description of the procedures to be followed, and identification of any procedures which are experimental.

(2) A description of any reasonably foreseeable risks or discomforts to the subject.

(3) A description of any benefits to the subject or to others which may reasonably be expected from the research.

(4) A disclosure of appropriate alternative procedures or courses of treatment, if any, that might be advantageous to the subject.

(5) A statement describing the extent, if any, to which confidentiality of records identifying the subject will be maintained and that notes the possibility that the Food and Drug Administration may inspect the records.

(6) For research involving more than minimal risk, an explanation as to whether any compensation and an explanation as to whether any medical treatments are available if injury occurs and, if so, what they consist of, or where further information may be obtained.

(7) An explanation of whom to contact for answers to pertinent questions about the research and research subjects' rights, and whom to contact in the event of a research-related injury to the subject.

(8) A statement that participation is voluntary, that refusal to participate will involve no penalty or loss of benefits to which the subject is otherwise entitled, and that the subject may discontinue participation at any time without penalty or loss of benefits to which the subject is otherwise entitled.

(b) *Additional elements of informed consent.* When appropriate, one or more of the following elements of information shall also be provided to each subject:

(1) A statement that the particular treatment or procedure may involve risks to the subject (or to the embryo or fetus, if the subject is or may become pregnant) which are currently unforeseeable.

(2) Anticipated circumstances under which the subject's participation may be terminated by the investigator without regard to the subject's consent.

(3) Any additional costs to the subject that may result from participation in the research.

(4) The consequences of a subject's decision to withdraw from the research and procedures for orderly termination of participation by the subject.

(5) A statement that significant new findings developed during the course of the research which may relate to the subject's willingness to continue participation will be provided to the subject.

(6) The approximate number of subjects involved in the study.

(c) The informed consent requirements in these regulations are not intended to preempt any applicable Federal, State, or local laws which require additional information to be disclosed for informed consent to be legally effective.

(d) Nothing in these regulations is intended to limit the authority of a physician to provide emergency medical care to the extent the physician is permitted to do so under applicable Federal, State, or local law.

§ 50.27 Documentation of informed consent.

(a) Except as provided in § 56.109(c), informed consent shall be documented by the use of a written consent form approved by the IRB and signed by the subject or the subject's legally authorized representative. A copy shall be given to the person signing the form.

(b) Except as provided in § 56.109(c), the consent form may be either of the following:

(1) A written consent document that embodies the elements of informed consent required by § 50.25. This form may be read to the subject or the subject's legally authorized representative, but, in any event, the investigator shall give either the subject or the representative adequate opportunity to read it before it is signed.

(2) A "short form" written consent document stating that the elements of informed consent required by § 50.25 have been presented orally to the subject or the subject's legally authorized representative. When this method is used, there shall be a witness to the oral presentation. Also, the IRB shall approve a written summary of what is to be said to the subject or the representative. Only the short form itself is to be signed by the subject or the representative. However, the witness shall sign both the short form and a copy of the summary, and the person actually obtaining the consent shall sign a copy of the summary. A copy of the summary shall be given to the subject or the representative in addition to a copy of the short form.

Subpart C—Protections Pertaining to Clinical Investigations Involving Prisoners as Subjects

EFFECTIVE DATE NOTE: At 46 FR 35085, July 7, 1981, the effective date of Subpart C was stayed until further notice.

§ 50.40 Applicability.

(a) The regulations in this subpart apply to all clinical investigations involving prisoners as subjects that are regulated by the Food and Drug Administration under sections 505(i), 507(d), or 520(g) of the Federal Food, Drug, and Cosmetic Act, as well as clinical investigations involving prisoners that support applications for research or marketing permits for products regulated by the Food and Drug Administration.

(b) Nothing in this subpart shall be construed as indicating that compliance with the procedures set forth herein will authorize research involving prisoners as subjects to the extent such research is limited or barred by applicable State or local law.

§ 50.42 Purpose.

Inasmuch as prisoners may be under constraints because of their incarceration which could affect their ability to make a truly voluntary and uncoerced decision whether or not to participate as subjects in research, it is the purpose of this subpart to provide additional safeguards for the protection of prisoners involved in activities to which this subpart is applicable.

§ 50.44 Restrictions on clinical investigations involving prisoners.

(a) Except as provided in § 50.44(b), clinical investigations regulated by the Food and Drug Administration under sections 505(i), 507(d), and 505(g) of the Federal Food, Drug, and Cosmetic Act, as well as clinical investigations that support applications for research or marketing permits for products regulated by the Food and Drug Administration may not involve prisoners as subjects.

(b) Clinical investigations that are regulated by the Food and Drug Administration under sections 505(i), 507(d), or 520(g) of the Federal Food, Drug, and Cosmetic Act, as well as clinical investigations that support applications for research or marketing permits for products regulated by the Food and Drug Administration, may involve prisoners as subjects only if the institution responsible for the conduct of the clinical investigation has certified to the Food and Drug Administration that the institutional review board has approved the clinical investigation under § 50.48; and

(1)(i) In the judgment of the Food and Drug Administration, the proposed clinical investigation involves solely research on practices both innovative and accepted, which have the intent and reasonable probability of improving, the health and well-being of the subjects;

(ii) In cases in which these studies require the assignment of prisoners in a manner consistent with protocols approved by the institutional review board to control groups that may not benefit from the research, the study may proceed only after the Food and Drug Administration has consulted with appropriate experts, including experts in penology, medicine, and ethics, and has published notice in the Federal Register of its intent to approve such research; or

(2) Research on conditions particularly affecting prisoners as a class (for example, vaccine trials and other research on hepatitis, which is much more prevalent in prisons than elsewhere) provided that the Food and Drug Administration has consulted with appropriate experts, including experts in penology, medicine, and ethics, and has published notice in the Federal Register of its intent to approve such research; subject to the approval of the Food and Drug Administration, prisoners may participate in the research even though they are assigned, in a manner consistent with protocols approved by the institutional review board, to control groups that may not benefit from the research.

§ 50.46 Composition of institutional review boards where prisoners are involved.

In addition to satisfying any other requirements governing institutional review boards set forth in this chapter, an institutional review board, in carrying out responsibilities under this part with respect to research covered by this subpart, shall also meet the following specific requirements:

(a) A majority of the institutional review board (exclusive of prisoner members) shall have no association with the prison(s) involved, apart from their membership on the institutional review board.

(b) At least one member of the institutional review board shall be a prisoner, or a prisoner advocate with appropriate background and experience to serve in that capacity, except that if a particular research project is reviewed by more than one institutional review board, only one institutional review board need satisfy this requirement.

§ 50.48 Additional duties of the institutional review boards where prisoners are involved.

(a) In addition to all other responsibilities prescribed for institutional review boards under this chapter, the institutional review board shall review clinical investigations covered by this subpart and approve such clinical investigations only if it finds that:

(1) The research under review represents one of the categories of research permitted under § 50.44(b) (1) and (2);

(2) Any possible advantages accruing to the prisoner through his or her participation in the clinical investigation, when compared to the general living conditions, medical care, quality of food, amenities, and opportunity for earnings in prison, are not of such a magnitude that his or her ability to weigh the risks of the clinical investigation against the value of such advantages in the limited-choice environment of the prison is impaired;

(3) The risks involved in the clinical investigation are commensurate with risks that would be accepted by nonprisoner volunteers;

(4) Procedures for the selection of subjects within the prison are fair to all prisoners and immune from arbitrary intervention by prison authorities or prisoners; unless the principal investigator provides to the institutional review board justification in

writing for following some other procedures, control subjects must be selected randomly from the group of available prisoners who meet the characteristics needed for that research project;

(5) Any information given to subjects is presented in language which is appropriate for the subject population;

(6) Adequate assurance exists that parole boards will not take into account a prisoner's participation in the clinical investigation in making decisions regarding parole, and each prisoner is clearly informed in advance that participation in the clinical investigation will have no effect on his or her parole; and

(7) Where the institutional review board finds there may be need for followup examination or care of participants after the end of their participation, adequate provision has been made for such examination or care, taking into account the varying lengths of individual prisoners' sentences, and for informing participants of this fact.

(b) The institutional review board shall carry out such other duties as may be assigned by the Food and Drug Administration.

(c) The institution shall certify to the Food and Drug Administration, in such form and manner as the Food and Drug Administration may require, that the duties of the institutional review board under this section have been fulfilled.

PART 56—INSTITUTIONAL REVIEW BOARDS

Subpart A—General Provisions

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AUTHORITY: Secs. 406, 408, 409, 501, 502, 503, 505, 506, 507, 510, 513-516, 518-520, 701(a), 706, and 801, Pub. L. 717, 52 Stat. 1049-1054 as amended, 1055, 1058 as amended, 55 Stat. 851 as amended, 59 Stat. 463 as amended, 68 Stat. 511-518 as amended, 72 Stat. 1785-1788 as amended, 74 Stat. 399-407 as amended, 76 Stat. 794-795 as amended, 90 Stat. 540-546, 560, 562-574 (21 U.S.C. 346, 346a, 348, 351, 352, 353, 355, 356, 357, 360, 360c-360f, 360h-360j, 371(a), 376, and 381), secs. 215, 301, 351, 354-360F, Pub. L. 410, 58 Stat. 690, 702 as amended, 82 Stat. 1173-1186 as amended (42 U.S.C. 216, 241, 262, 263b-263n).

SOURCE: 46 FR 8975, Jan. 27, 1981, unless otherwise noted.

Subpart A—General Provisions

§ 56.101 Scope.

(a) This part contains the general standards for the composition, operation, and responsibility of an Institutional Review Board (IRB) that reviews clinical investigations regulated by the Food and Drug Administration under sections 505(i), 507(d), and 520(g) of the act, as well as clinical investigations that support applications for research or marketing permits for products regulated by the Food and Drug Administration, including food and color additives, drugs for human use, medical devices for human use, biological products for human use, and electronic products. Compliance with this part is intended to protect the rights and welfare of human subjects involved in such investigations.

(b) References in this part to regulatory sections of the Code of Federal Regulations are to Chapter I of Title 21, unless otherwise noted.

§ 56.102 Definitions.

As used in this part:

(a) "Act" means the Federal Food, Drug, and Cosmetic Act, as amended (secs. 201-902, 52 Stat. 1040 et seq., as amended (21 U.S.C. 321-392)).

(b) "Application for research or marketing permit" includes:

(1) A color additive petition, described in Part 71.

(2) Data and information regarding a substance submitted as part of the procedures for establishing that a substance is generally recognized as safe for a use which results or may reasonably be expected to result, directly or indirectly, in its becoming a component or otherwise affecting the characteristics of any food, described in § 170.35.

(3) A food additive petition, described in Part 171.

(4) Data and information regarding a food additive submitted as part of the procedures regarding food additives permitted to be used on an interim basis pending additional study, described in § 180.1.

(5) Data and information regarding a substance submitted as part of the procedures for establishing a tolerance for unavoidable contaminants in food and food-packaging materials, described in section 406 of the act.

(6) A "Notice of Claimed Investigational Exemption for a New Drug" described in Part 312.

(7) A new drug application, described in Part 314.

(8) Data and information regarding the bioavailability or bioequivalence of drugs for human use submitted as part of the procedures for issuing, amending, or repealing a bioequivalence requirement, described in Part 320.

(9) Data and information regarding an over-the-counter drug for human use submitted as part of the procedures for classifying such drugs as generally recognized as safe and effective and not misbranded, described in Part 330.

(10) Data and information regarding an antibiotic drug submitted as part of the procedures for issuing, amending, or repealing regulations for such drugs, described in Part 430.

(11) An application for a biological product license, described in Part 601.

(12) Data and information regarding a biological product submitted as part of the procedures for determining that licensed biological products are safe and effective and not misbranded, as described in Part 601.

(13) An "Application for an Investigational Device Exemption," described in Parts 812 and 813.

(14) Data and information regarding a medical device for human use submitted as part of the procedures for classifying such devices, described in Part 860.

(15) Data and information regarding a medical device for human use submitted as part of the procedures for establishing, amending, or repealing a standard for such device, described in Part 861.

(16) An application for premarket approval of a medical device for human use, described in section 515 of the act.

(17) A product development protocol for a medical device for human use, described in section 515 of the act.

(18) Data and information regarding an electronic product submitted as part of the procedures for establishing, amending, or repealing a standard for such products, described in section 358 of the Public Health Service Act.

(19) Data and information regarding an electronic product submitted as part of the procedures for obtaining a variance from any electronic product performance standard, as described in § 1010.4.

(20) Data and information regarding an electronic product submitted as part of the procedures for granting, amending, or extending an exemption from a radiation safety performance standard, as described in § 1010.5.

(21) Data and information regarding an electronic product submitted as

part of the procedures for obtaining an exemption from notification of a radiation safety defect or failure of compliance with a radiation safety performance standard, described in Subpart D of Part 1003.

(c) "Clinical investigation" means any experiment that involves a test article and one or more human subjects, and that either must meet the requirements for prior submission to the Food and Drug Administration under section 505(i), 507(d), or 520(g) of the act, or need not meet the requirements for prior submission to the Food and Drug Administration under these sections of the act, but the results of which are intended to be later submitted to, or held for inspection by, the Food and Drug Administration as part of an application for a research or marketing permit. The term does not include experiments that must meet the provisions of Part 58, regarding nonclinical laboratory studies. The terms "research," "clinical research," "clinical study," "study," and "clinical investigation" are deemed to be synonymous for purposes of this part.

(d) "Emergency use" means the use of a test article on a human subject in a life-threatening situation in which no standard acceptable treatment is available, and in which there is not sufficient time to obtain IRB approval.

(e) "Human subject" means an individual who is or becomes a participant in research, either as a recipient of the test article or as a control. A subject may be either a healthy individual or a patient.

(f) "Institution" means any public or private entity or agency (including Federal, State, and other agencies). The term "facility" as used in section 520(g) of the act is deemed to be synonymous with the term "institution" for purposes of this part.

(g) "Institutional Review Board (IRB)" means any board, committee, or other group formally designated by an institution to review, to approve the initiation of, and to conduct periodic review of, biomedical research involving human subjects. The primary purpose of such review is to assure the protection of the rights and welfare of the human subjects. The term has the same meaning as the phrase "institutional review committee" as used in section 520(g) of the act.

(h) "Investigator" means an individual who actually conducts a clinical investigation (i.e., under whose immediate direction the test article is administered or dispensed to, or used involving, a subject) or, in the event of an investigation conducted by a team of individuals, is the responsible leader of that team.

(i) "Minimal risk" means that the risks of harm anticipated in the proposed research are not greater, considering probability and magnitude, than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests.

(j) "Sponsor" means a person or other entity that initiates a clinical investigation, but that does not actually conduct the investigation, i.e., the test article is administered or dispensed to, or used involving, a subject under the immediate direction of another individual. A person other than an individual (e.g., a corporation or agency) that uses one or more of its own employees to conduct an investigation that it has initiated is considered to be a sponsor (not a sponsor-investigator), and the employees are considered to be investigators.

(k) "Sponsor-investigator" means an individual who both initiates and actually conducts, alone or with others, a clinical investigation, i.e., under whose immediate direction the test article is administered or dispensed to, or used involving, a subject. The term does not include any person other than an individual, e.g., it does not include a corporation or agency. The obligations of a sponsor-investigator under this part include both those of a sponsor and those of an investigator.

(l) "Test article" means any drug for human use, biological product for human use, medical device for human use, human food additive, color additive, electronic product, or any other article subject to regulation under the act or under sections 351 or 354-360F of the Public Health Service Act.

§ 56.103 Circumstances in which IRB review is required.

(a) Except as provided in §§ 56.104 and 56.105, any clinical investigation which must meet the requirements for prior submission (as required in Parts 312, 812, and 813) to the Food and Drug Administration shall not be initiated unless that investigation has been reviewed and approved by, and remains subject to continuing review by, an IRB meeting the requirements of this part.

(b) Except as provided in §§ 56.104 and 56.105, the Food and Drug Administration may decide not to consider in support of an application for a research or marketing permit any data or information that has been derived from a clinical investigation that has not been approved by, and that was not subject to initial and continuing review by, an IRB meeting the requirements of this part. The determination that a clinical investigation may not be considered in support of an application for a research or marketing permit does not, however, relieve the applicant for such a permit of any obligation under any other applicable regulations to submit the results of the investigation to the Food and Drug Administration.

(c) Compliance with these regulations will in no way render inapplicable pertinent Federal, State, or local laws or regulations.

[46 FR 8975, Jan. 27, 1981; 46 FR 14340, Feb. 27, 1981]

§ 56.104 Exemptions from IRB requirement.

The following categories of clinical investigations are exempt from the requirements of this part for IRB review:

(a) Any investigation which commenced before July 27, 1981 and was subject to requirements for IRB review under FDA regulations before that date, provided that the investigation remains subject to review of an IRB which meets the FDA requirements in effect before July 27, 1981.

(b) Any investigation commenced before July 27, 1981 and was not otherwise subject to requirements for IRB review under Food and Drug Administration regulations before that date.

(c) Emergency use of a test article, provided that such emergency use is reported to the IRB within 5 working days. Any subsequent use of the test article at the institution is subject to IRB review.

§ 56.105 Waiver of IRB requirement.

On the application of a sponsor or sponsor-investigator, the Food and Drug Administration may waive any of the requirements contained in these regulations, including the requirements for IRB review, for specific research activities or for classes of research activities, otherwise covered by these regulations.

Subpart B—Organization and Personnel

§ 56.107 IRB membership.

(a) Each IRB shall have at least five members, with varying backgrounds to promote complete and adequate review of research activities commonly conducted by the institution. The IRB shall be sufficiently qualified through the experience and expertise of its members, and the diversity of the members' backgrounds including consideration of the racial and cultural backgrounds of members and sensitivity to such issues as community attitudes, to promote respect for its advice and counsel in safeguarding the rights and welfare of human subjects. In addition to possessing the professional competence necessary to review specific research activities, the IRB shall be able to ascertain the acceptability of proposed research in terms of institutional commitments and regulations, applicable law, and standards of professional conduct and practice. The IRB shall therefore include persons knowledgeable in these areas. If an IRB regularly reviews research that involves a vulnerable category of subjects, including but not limited to subjects covered by other parts of this chapter, the IRB should include one or more individuals who are primarily concerned with the welfare of these subjects.

(b) No IRB may consist entirely of men, or entirely of women, or entirely of members of one profession.

(c) Each IRB shall include at least one member whose primary concerns are in nonscientific areas; for example: lawyers, ethicists, members of the clergy.

(d) Each IRB shall include at least one member who is not otherwise affiliated with the institution and who is not part of the immediate family of a person who is affiliated with the institution.

(e) No IRB may have a member participate in the IRB's initial or continuing review of any project in which the member has a conflicting interest, except to provide information requested by the IRB.

(f) An IRB may, in its discretion, invite individuals with competence in special areas to assist in the review of complex issues which require expertise beyond or in addition to that available on the IRB. These individuals may not vote with the IRB.

Subpart C—IRB Functions and Operations

§ 56.108 IRB functions and operations.

In order to fulfill the requirements of these regulations, each IRB shall:

(a) Follow written procedures (1) for conducting its initial and continuing review of research and for reporting its findings and actions to the investigator and the institution, (2) for determining which projects require review more often than annually and which projects need verification from sources other than the investigators that no material changes have occurred since previous IRB review, (3) for insuring prompt reporting to the IRB of changes in a research activity, (4) for insuring that changes in approved research, during the period for which IRB approval has already been given, may not be initiated without IRB review and approval except where necessary to eliminate apparent immediate hazards to the human subjects; and (5) for insuring prompt reporting to the IRB of unanticipated problems involving risks to subjects or others.

(b) Except when an expedited review procedure is used (see § 56.110), review proposed research at convened meetings at which a majority of the members of the IRB are present, including at least one member whose primary concerns are in nonscientific areas. In order for the research to be approved, it shall receive the approval of a majority of those members present at the meeting.

(c) Be responsible for reporting to the appropriate institutional officials and the Food and Drug Administration any serious or continuing noncompliance by investigators with the requirements and determinations of the IRB.

§ 56.109 IRB review of research.

(a) An IRB shall review and have authority to approve, require modifications in (to secure approval), or disapprove all research activities covered by these regulations.

(b) An IRB shall require that information given to subjects as part of informed consent is in accordance with § 50.25. The IRB may require that information, in addition to that specifically mentioned in § 50.25, be given to the subjects when in the IRB's judgment the information would meaningfully add to the protection of the rights and welfare of subjects.

(c) An IRB shall require documentation of informed consent in accordance with § 50.27, except that the IRB may, for some or all subjects, waive the requirement that the subject or the subject's legally authorized representative sign a written consent form if it finds that the research presents no more than minimal risk of harm to subjects and involves no procedures for which written consent is normally required outside the research context. In cases where the documentation requirement is waived, the IRB may require the investigator to provide subjects with a written statement regarding the research.

(d) An IRB shall notify investigators and the institution in writing of its decision to approve or disapprove the proposed research activity, or of modifications required to secure IRB approval of the research activity. If the IRB decides to disapprove a research activity, it shall include in its written notification a statement of the reasons for its decision and give the investigator an opportunity to respond in person or in writing.

(e) An IRB shall conduct continuing review of research covered by these regulations at intervals appropriate to the degree of risk, but not less than once per year, and shall have authority to observe or have a third party observe the consent process and the research.

§ 56.110 Expedited review procedures for certain kinds of research involving no more than minimal risk, and for minor changes in approved research.

(a) The Food and Drug Administration has established, and published in the FEDERAL REGISTER, a list of categories of research that may be reviewed by the IRB through an expedited review procedure. The list will be amended, as appropriate, through periodic republication in the FEDERAL REGISTER.

(b) An IRB may review some or all of the research appearing on the list through an expedited review procedure, if the research involves no more than minimal risk. The IRB may also use the expedited review procedure to review minor changes in previously approved research during the period for which approval is authorized. Under an expedited review procedure, the review may be carried out by the IRB chairperson or by one or more experienced reviewers designated by the chairperson from among members of the IRB. In reviewing the research, the reviewers may exercise all of the authorities of the IRB except that the reviewers may not disapprove the research. A research activity may be disapproved only after review in accordance with the non-expedited procedure set forth in § 56.108(b).

(c) Each IRB which uses an expedited review procedure shall adopt a method for keeping all members advised of research proposals which have been approved under the procedure.

(d) The Food and Drug Administration may restrict, suspend, or terminate an institution's or IRB's use of the expedited review procedure when necessary to protect the rights or welfare of subjects.

§ 56.111 Criteria for IRB approval of research.

(a) In order to approve research covered by these regulations the IRB shall determine that all of the following requirements are satisfied:

(1) Risks to subjects are minimized: (i) By using procedures which are consistent with sound research design and which do not unnecessarily expose subjects to risk, and (ii) whenever appropriate, by using procedures already being performed on the subjects for diagnostic or treatment purposes.

(2) Risks to subjects are reasonable in relation to anticipated benefits, if any, to subjects, and the importance of the knowledge that may be expected to result. In evaluating risks and benefits, the IRB should consider only those risks and benefits that may result from the research (as distinguished from risks and benefits of therapies that subjects would receive even if not participating in the research). The IRB should not consider possible long-range effects of applying knowledge gained in the research (for example, the possible effects of the research on public policy) as among those research risks that fall within the purview of its responsibility.

(3) Selection of subjects is equitable. In making this assessment, the IRB should take into account the purposes of the research and the setting in which the research will be conducted.

(4) Informed consent will be sought from each prospective subject or the subject's legally authorized representative, in accordance with and to the extent required by Part 50.

(5) Informed consent will be appropriately documented, in accordance with and to the extent required by § 50.27.

(6) Where appropriate, the research plan makes adequate provision for monitoring the data collected to ensure the safety of subjects.

(7) Where appropriate, there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data.

(b) Where some or all of the subjects are likely to be vulnerable to coercion or undue influence, such as persons with acute or severe physical or mental illness, or persons who are economically or educationally disadvantaged, appropriate additional safeguards have been included in the study to protect the rights and welfare of these subjects.

§ 56.112 Review by institution.

Research covered by these regulations that has been approved by an IRB may be subject to further appropriate review and approval or disapproval by officials of the institution. However, those officials may not approve the research if it has not been approved by an IRB.

§ 56.113 Suspension or termination of IRB approval of research.

An IRB shall have authority to suspend or terminate approval of research that is not being conducted in accordance with the IRB's requirements or that has been associated with unexpected serious harm to subjects. Any suspension or termination of approval shall include a statement of the reasons for the IRB's action and shall be reported promptly to the investigator, appropriate institutional officials, and the Food and Drug Administration.

§ 56.114 Cooperative research.

In complying with these regulations, institutions involved in multi-institutional studies may use joint review, reliance upon the review of another qualified IRB, or similar arrangements aimed at avoidance of duplication of effort.

Subpart D—Records and Reports

§ 56.115 IRB records.

(a) An institution, or where appropriate an IRB, shall prepare and maintain adequate documentation of IRB activities, including the following:

(1) Copies of all research proposals reviewed, scientific evaluations, if any, that accompany the proposals, approved sample consent documents, progress reports submitted by investigators, and reports of injuries to subjects.

(2) Minutes of IRB meetings which shall be in sufficient detail to show attendance at the meetings; actions taken by the IRB; the vote on these actions including the number of members voting for, against, and abstaining; the basis for requiring changes in or disapproving research; and a written summary of the discussion of controverted issues and their resolution.

(3) Records of continuing review activities.

(4) Copies of all correspondence between the IRB and the investigators.

(5) A list of IRB members identified by name; earned degrees; representative capacity; indications of experience such as board certifications, licenses, etc., sufficient to describe each member's chief anticipated contributions to IRB deliberations; and any employment or other relationship between each member and the institution; for example: full-time employee, part-time employee, a member of governing panel or board, stockholder, paid or unpaid consultant.

(6) Written procedures for the IRB as required by § 56.108(a).

(7) Statements of significant new findings provided to subjects, as required by § 50.25.

(b) The records required by this regulation shall be retained for at least 3 years after completion of the research, and the records shall be accessible for inspection and copying by authorized representatives of the Food and Drug Administration at reasonable times and in a reasonable manner.

(c) The Food and Drug Administration may refuse to consider a clinical investigation in support of an application for a research or marketing permit if the institution or the IRB that reviewed the investigation refuses to allow an inspection under this section.

Subpart E—Administrative Actions for Noncompliance

§ 56.120 Lesser administrative actions.

(a) If apparent noncompliance with these regulations in the operation of an IRB is observed by an FDA investigator during an inspection, the inspector will present an oral or written summary of observations to an appropriate representative of the IRB. The

Food and Drug Administration may subsequently send a letter describing the noncompliance to the IRB and to the parent institution. The agency will require that the IRB or the parent institution respond to this letter within a time period specified by FDA and describe the corrective actions that will be taken by the IRB, the institution, or both to achieve compliance with these regulations.

(b) On the basis of the IRB's or the institution's response, FDA may schedule a reinspection to confirm the adequacy of corrective actions. In addition, until the IRB or the parent institution takes appropriate corrective action, the agency may:

(1) Withhold approval of new studies subject to the requirements of this part that are conducted at the institution or reviewed by the IRB;

(2) Direct that no new subjects be added to ongoing studies subject to this part;

(3) Terminate ongoing studies subject to this part when doing so would not endanger the subjects; or

(4) When the apparent noncompliance creates a significant threat to the rights and welfare of human subjects, notify relevant State and Federal regulatory agencies and other parties with a direct interest in the agency's action of the deficiencies in the operation of the IRB.

(c) The parent institution is presumed to be responsible for the operation of an IRB, and the Food and Drug Administration will ordinarily direct any administrative action under this subpart against the institution. However, depending on the evidence of responsibility for deficiencies, determined during the investigation, the Food and Drug Administration may restrict its administrative actions to the IRB or to a component of the parent institution determined to be responsible for formal designation of the IRB.

§ 56.121 Disqualification of an IRB or an institution.

(a) Whenever the IRB or the institution has failed to take adequate steps to correct the noncompliance stated in the letter sent by the agency under § 56.120(a), and the Commissioner of Food and Drugs determines that this noncompliance may justify the disqualification of the IRB or of the parent institution, the Commissioner will institute proceedings in accordance with the requirements for a regulatory hearing set forth in Part 16.

(b) The Commissioner may disqualify an IRB or the parent institution if the Commissioner determines that:

(1) The IRB has refused or repeatedly failed to comply with any of the regulations set forth in this part, and

(2) The noncompliance adversely affects the rights or welfare of the human subjects in a clinical investigation.

(c) If the Commissioner determines that disqualification is appropriate, the Commissioner will issue an order that explains the basis for the determination and that prescribes any actions to be taken with regard to ongoing clinical research conducted under the review of the IRB. The Food and Drug Administration will send notice of the disqualification to the IRB and the parent institution. Other parties with a direct interest, such as sponsors and clinical investigators, may also be sent a notice of the disqualification. In addition, the agency may elect to publish a notice of its action in the FEDERAL REGISTER.

(d) The Food and Drug Administration will not approve an application for a research permit for a clinical investigation that is to be under the review of a disqualified IRB or that is to be conducted at a disqualified institution, and it may refuse to consider in support of a marketing permit the data from a clinical investigation that was reviewed by a disqualified IRB as conducted at a disqualified institution, unless the IRB or the parent institution is reinstated as provided in § 56.123.

§ 56.122 Public disclosure of information regarding revocation.

A determination that the Food and Drug Administration has disqualified an institution and the administrative record regarding that determination are disclosable to the public under Part 20.

§ 56.123 Reinstatement of an IRB or an institution.

An IRB or an institution may be reinstated if the Commissioner determines, upon an evaluation of a written submission from the IRB or institution that explains the corrective action that the institution or IRB plans to take, that the IRB or institution has provided adequate assurance that it will operate in compliance with the standards set forth in this part. Notification of reinstatement shall be provided to all persons notified under § 56.121(c).

§ 56.124 Actions alternative or additional to disqualification.

Disqualification of an IRB or of an institution is independent of, and neither in lieu of nor a precondition to, other proceedings or actions authorized by the act. The Food and Drug Administration may, at any time, through the Department of Justice institute any appropriate judicial proceedings (civil or criminal) and any other appropriate regulatory action, in addition to or in lieu of, and before, at the time of, or after, disqualification. The agency may also refer pertinent matters to another Federal, State, or local government agency for any action that that agency determines to be appropriate.

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. 85D–0291]

Guidance for the Emergency Use of Unapproved Medical Devices; Availability

AGENCY: Food and Drug Administration.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) is announcing guidance, developed by FDA's Center for Devices and Radiological Health (CDRH), with respect to those emergency situations in which the agency would not object to a physician's using a potentially life-saving medical device for a use for which the device ordinarily is required to have, but does not have, an approved application for premarket approval or an investigational device exemption. The guidance is contained in a document entitled "guidance for the Emergency Use of Unapproved Medical Devices."

DATE: Comments by December 23, 1985.

ADDRESSES: Requests for single copies of the guidance document should be sent to Tracy A. Summers, Center for Devices and Radiological Health (HFZ–84), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857. Written comments to the Dockets Management Branch (HFA–305), Food and Drug Administration, Rm. 4–62, 5600 Fishers Lane, Rockville, MD 20857.

FOR FURTHER INFORMATION CONTACT: Halyna Breslawec, Center for Devices and Radiological Health (HFZ–403), Food and Drug Administration, 8757 Georgia Ave., Silver Spring, MD 20910, 301–427–8162.

SUPPLEMENTARY INFORMATION: FDA is making available for comment guidance concerning the emergency use of an unapproved medical device. For the purpose of the guidance, an unapproved medical device is a device which, under section 501(f) of the Federal Food, Drug, and Cosmetic Act (the act) (21 U.S.C. 351(f)), is subject to premarket approval to provide reasonable assurance of its safety and effectiveness for the purpose, condition, or use for which it is intended but which does not have in effect for such purpose, condition, or use either (1) a premarket approval application (PMA) under section 515 of the act (21 US.C. 360e) or (2) an Application for an Investigational Device Exemption (IDE) under section 520(g) of the act (21 U.S.C. 360j(g)) and Part 812 of FDA's regulations (21 CFR Part 812). In short, an unapproved device is a device that is utilized for a purpose, condition, or use for which the device ordinarily is required to have, but does not have, an approved PMA or IDE.

The guidance also concerns the emergency use by a physician of a device that is the subject of an approved IDE when the physician (i) is an investigator for the sponsor of the approved application but does not use the device in accordance with the terms and conditions of the application or (ii) is not an investigator.

An unapproved medical device may be used in human subjects only if it is approved for investigational use under an IDE and is used by an investigator for the sponsor in accordance with the terms and conditions of the application. IDE applications are reviewed by FDA promptly, and are deemed approved 30 days after their receipt by FDA, unless FDA notifies the sponsor that the investigation may not begin. FDA recognizes, however, that during the early phases of device design, development, and testing, an emergency may arise where, in a physician's judgment, an approved device would offer the only alternative for saving the life of a dying patient. Such a situation occurred recently with the use of an artificial heart. Realizing that there is a need for guidance on the use of unapproved devices in similar situations, CDRH developed a document that provides guidance to the physician with respect to emergency situations that require the use of such devices.

The guidance document discusses: (1) The criteria necessary for a situation to be considered an emergency; (2) the patient protection procedures the physician should follow before using an unapproved device in an emergency situation; (3) the procedures the physician should follow after using an unapproved device in an emergency situation; and (4) the situations in which use of an unapproved medical device is not justified, even though an emergency exists. The document also provides guidance to the sponsor of an approved IDE when the device that is the subject of the approved application is used in an emergency by a physician who is an investigator for the sponsor but who does not use the device in accordance with the terms and conditions of the application, or by a physician who is not an investigator. Finally, the document provides guidance to the physician in either of those circumstances.

FDA expects physicians to make the determination as to whether the criteria for emergency use of an unapproved medical device set forth in the guidance have been met. FDA will consider taking regulatory action if an unapproved device is used in inappropriate situations.

For the convenience of interested persons, FDA is including in this notice the entire guidance document:

Guidance for the Emergency Use of Unapproved Medical Devices

This guidance applies to the emergency use of an unapproved medical device. For the purpose of the guidance, an unapproved medical device is a device that is utilized for a purpose, condition, or use for which the device requires, but does not have, an approved application for premarket approval under section 515 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 360e) or an approved Application for an Investigational Device Exemption (IDE) under section 520(g) of the act (21 U.S.C. 360j(g)) and Part 812 of FDA's regulations (21 CFR Part 812).

An unapproved device may be used in human subjects only if it is approved for clinical testing under an IDE. An emergency need to use an unapproved device may occur when an IDE for the device does not exist, when a physician wants to use the device in a way not approved under the IDE, or when a physician or institution is not approved under the IDE.

In an orderly developmental process, the device's developer—a physician, scientist, or manufacturer—anticipates the need to conduct clinical studies and uses the IDE to ensure that adequate preclinical testing has been done, that the appropriate subjects will be selected, that subjects participate only after providing informed consent, that the device will be used properly, that subjects will be monitored adequately after the device is used, and that complete scientific data will be collected promptly. These data form the basis for subsequent marketing approval of the device.

The Food and Drug Administration (FDA) recognizes that even during the earliest phases of device design, development, and testing, emergencies arise where an unapproved device offers the only alternative for saving the life of a dying patient, but an IDE has not yet been approved for the device or the use, or an IDE has been approved but the physician who wishes to use the device is not an investigator under the IDE. Using its enforcement discretion, FDA will not object if a physician chooses to use an unapproved device in such an emergency, provided that the physician later justifies to FDA that an emergency actually existed.

Each of the following conditions should exist for a situation to be considered an emergency:

1. The patient is in a life-threatening condition that needs immediate treatment:

2. No generally acceptable alternative for treating the patient is available; and

3. Because of the immediate need to use the device, there is no time to use existing procedures to get FDA approval for the use.

FDA expects the physician to determine whether these criteria have been met, to assess the potential for benefits from the unapproved use of the device, and to have substantial reason to believe that benefits will exist. FDA further expects the physician not to conclude that an "emergency" situation exists in advance of the time when treatment may be needed based solely on the expectation that IDE approval procedures may require more time than remains. Physicians should be aware that FDA expects them to exercise reasonable foresight with respect to potential emergencies and to make appropriate arrangements under the IDE procedures far enough in advance to avoid creating a situation in which such arrangements are impracticable.

In the event that a device is used in circumstances meeting the criteria listed above, FDA would expect the physician to follow as many patient protection procedures as possible. These include obtaining:

1. An independent assessment by an uninvolved physician;

2. Informed consent from the patient or a legal representative;

3. Institutional clearance as specified by institutional policies;

4. The Institutional Review Board (IRB) chairperson's concurrence, and

5. Authorization from the sponsor, if an approved IDE for the device exists.

FDA would not object if an unapproved device were shipped without FDA approval to a physician who claims to be faced with, and describes, the kind of emergency situation discussed above. The person shipping the device should notify FDA—by telephone (301–427–8162)—immediately after shipment is made. An unapproved device may not be shipped in anticipation of an emergency.

After an unapproved device is used in an emergency, the physician should:

1. Notify the IRB and otherwise comply with provisions of the IRB regulations (21 CFR Part 56) and the informed consent regulations (21 CFR Part 50);

2. Evaluate the likelihood of a similar need for the device in the future: If it is likely, immediately initiate efforts to obtain IRB approval and an approved IDE for the device's subsequent use;

3. If an IDE exists, notify the sponsor of the emergency use of the device: The sponsor must comply with the reporting requirements of the IDE regulations; and

4. If an IDE does not exist, notify FDA of the emergency use of the device and provide FDA with a written summary of the conditions constituting the emergency, patient protection measures, and any scientific results.

Subsequent use of the device in an emergency situation may not occur unless the physician or another person obtains approval of an IDE for the device and its use. If an IDE application for subsequent use has been filed with FDA and FDA disapproves the IDE application, the device may not be used even if the circumstances constituting an emergency exist. Developers of devices that could be used in emergencies should anticipate the likelihood of emergency uses and should obtain an approved IDE. FDA will consider taking regulatory action if an unapproved device is used in inappropriate situations.

CDRH developed this guidance in response to a situation concerning the emergency use of an unapproved cardiovascular device. CDRH will apply this guidance to other types of potentially life-saving unapproved devices in emergency situations. In all situations in which the use of an unapproved device would not meet the criteria for emergency use under this guidance, such unapproved device may not be used without an approved IDE.

Interested persons may, on or before December 23, 1985, submit written comments to the Dockets Management Branch (address above). Two copies of any comments should be submitted, except that individuals may submit one copy. Comments are to be identified with the docket number found in brackets in the heading of this document. FDA will consider any comments received. The document and comments received may be seen in the Dockets Management Branch between 9 a.m. and 4 p.m., Monday through Friday.

Dated: October 12, 1985.

Frank E. Young,

Commissioner of Food and Drugs.

[FR Doc 85–25063 Filed 10–21–85; 8:45 am]

BILLING CODE 4160-01-M

GUIDELINE FOR PREPARING NOTICES OF AVAILABILITY OF INVESTIGATIONAL MEDICAL DEVICES

This guideline is intended to clarify Section 812.7 of 21 CFR Part 812, the regulations providing procedures for investigational device exemptions (OMB control number 0910-0078), and Section 813.50 of 21 CFR Part 813, the regulations providing procedures for investigational device exemptions for intraocular lenses (OMB control number 0910-0067). These two sections prohibit the promotion or test marketing of investigational medical devices. Any person wishing to make known through a notice, publication, display, mailing, exhibit, announcement, or oral presentation the availability of an investigational device for the purpose of obtaining clinical investigators to participate in a clinical study involving human subjects should:

1. Announce the availability of the device only in medical or scientific publications or at medical or scientific conferences whose readership or audience is composed primarily of experts qualified by scientific training and experience to investigate the safety and effectiveness of devices.

2. State in clear terms that the purpose is **only** to obtain investigators and not to make the device generally available. Enrolling more investigators or subjects than necessary to evaluate the safety and effectiveness of the device will be considered promotion or commercialization of the device. In addition, promoting the availability of the device to obtain additional sponsors may be considered promotion or commercialization of the device.

3. Limit the information presented in any notice of availability to the following: the name and address of the sponsor, how to apply to be an investigator, and how to obtain the device for investigational use. The notice should further list the investigator's responsibilities during the course of the investigation; namely, to await Institutional Review Board (IRB) and Food and Drug Administration (FDA) approval before allowing any subject to participate, to obtain informed consent from subjects, to permit the device to be used only with subjects under the investigator's supervision, to report adverse reactions, to keep accurate records, and, more generally, to conduct the investigation in accordance with the signed agreement with the sponsor, the investigational plan, FDA's regulations, and whatever conditions of approval are imposed by the reviewing IRB or FDA.

4. Use direct mailing for the sole purpose of soliciting qualified experts to conduct investigations. (Note: An undirected mass mailing will not be considered an appropriate means of soliciting clinical investigators. Such a mailing will be considered promotional.)

5. Include the following statement displayed prominently and in printing at least as large as the largest printing in the notice: "**Caution - Investigational Device, Limited By Federal (or United States) Law to Investigational Use.**" (Note: a clear, unequivocal statement that the device is under investigation and is available only for investigational use is to be made in oral presentations.)

6. Make only objective statements concerning the physical nature of the device.

7. Ensure that no claims are made which state or imply, directly or indirectly, that the device is reliable, durable, dependable, safe, or effective for the purposes under investigation or that the device is in any way superior to any other device.

8. Not present comparative descriptions of the device with other devices but may include reasonably-sized drawings or photographs of the device.

9. Not include information regarding pricing data but may include information stating where such data may be obtained. A sponsor or investigator should not offer volume discounts for an investigational device. FDA would regard such discounts as the promotion of an investigational device.

GUIDELINE FOR THE MONITORING
OF
CLINICAL INVESTIGATIONS

JANUARY 1988

Comments on the contents of this guideline are invited and should be addressed to the following office and identified with the docket number:

Dockets Management Branch (HFA-305)
Docket Number-82D-0322
Room 4-62
5600 Fishers Lane
Rockville, Maryland 20857

For copies of, or further information regarding, the guideline please contact:

Bioresearch Program Coordinator (HFC-230)
Food and Drug Administration
5600 Fishers Lane
Rockville, Maryland 20857

GUIDELINE FOR THE MONITORING
OF
CLINICAL INVESTIGATIONS

PURPOSE

The purpose of this guideline is to present acceptable approaches to monitoring clinical investigations. Existing requirements for sponsors of clinical investigations involving new drugs for humans and animal use (including biological products for human use) and medical devices under 21 CFR Parts 312 and 511, and 812 and 813, respectively, require that a sponsor monitor the progress of a clinical investigation. The monitoring functions may be performed by the sponsor or their own employees or may be delegated to a contract research organization as defined under 21 CFR 312.3. Proper monitoring is necessary to assure adequate protection of the rights of human subjects and the safety of all subjects involved in clinical investigations and the quality and integrity of the resulting data submitted to the Food and Administration (FDA).

INTRODUCTION

This guideline, issued under 21 CFR 10.90, reflects principles recognized by the scientific community as desirable approaches to monitoring clinical research involving human and animal subjects. These principles are not legal requirements but represent a standard of practice that is acceptable to FDA. A sponsor may rely upon this guideline or may develop different procedures. A sponsor who selects different procedures for monitoring a clinical investigation may, but is not required to, submit those procedures to FDA for review and comment to avoid the possibility of employing monitoring procedures that FDA might later determine to be inadequate. Sponsors wishing to obtain such a review should contact FDA's Bioresearch Program Coordinator (HFC-230), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857.

FDA may amend this guideline from time to time on the basis of comments submitted by interested persons or information obtained from agency inspections of sponsors, monitors, and investigators.

A. Selection of a Monitor

A sponsor may designate one or more appropriately trained and qualified individuals to monitor the progress of a clinical investigation. Physicians, veterinarians, clinical research associates, paramedical personnel, nurses, and engineers may be acceptable monitors depending on the type of product involved in the study. A monitor need not be a person qualified to diagnose and treat the disease or other condition for which the test article is under investigation, but somewhere in the direct line of review of the study data there should be a person so qualified.

For any given study, the factors that should be considered in determining the number of monitors and the education, training, or expertise necessary should include:

- The number of investigators conducting the study.
- The number and location of the facilities in which the study is being conducted.

- The type of product involved in the study (i.e., drug for human use, drug for animal use, medical device).
- The complexity of the study.
- The nature of the disease or other condition under study.

B. Written Monitoring Procedures

A sponsor should establish written procedures for monitoring clinical investigations to assure the quality of the study and to assure that each person involved in the monitoring process carries out his or her duties. A single written monitoring procedure need not be developed for each clinical investigation. Rather, a standardized, written procedure, sufficiently detailed to cover the general aspects of clinical investigations, may be used as a basic monitoring plan and supplemented by more specific or additional monitoring procedures tailored to the individual clinical investigations.

C. Preinvestigation Visits

A sponsor is responsible for assuring, through personal contact between the monitor and each investigator, that the investigator clearly understands and accepts the obligations incurred in undertaking a clinical investigation.

Prior to the initiation of a clinical investigation, the monitor should visit the site of the clinical investigation to assure that the investigator:

- Understands the investigational status of the test article and the requirements for its accountability.
- Understands the nature of the protocol or investigational plan.
- Understands the requirements for an adequate and well-controlled study.
- Understands and accepts his or her obligations to conduct the clinical investigation in accordance with 21 CFR Parts 312, 511, 812, 813, or any other applicable regulations.
- Understands and accepts his or her obligations to obtain informed consent in accordance with 21 CFR Part 50. The monitor should review a specimen of each consent document to be used by the investigator to assure that reasonable foreseeable risks are adequately explained.
- Understands and accepts his or her obligation to obtain IRB review and approval of a clinical investigation before the investigation may be initiated and to ensure continuing review of the study by the IRB in accordance with 21 CFR Part 56, and to keep the sponsor informed of such IRB approval and subsequent IRB actions concerning the study.
- Has access to an adequate number of suitable subjects to conduct the investigation.
- Has adequate facilities for conducting the clinical investigation.
- Has sufficient time from other obligations to carry out the responsibilities to which the investigator is committed by applicable regulations.

D. Periodic Visits

A sponsor is responsible for assuring throughout the clinical investigation that the investigator's obligations, as set forth in applicable regulations, are being fulfilled and that the facilities used in the clinical investigation continue to be acceptable. The most effective way to achieve this assurance is to maintain personal contact between the monitor and the investigator throughout the clinical investigation. The monitor should visit the investigator at the site of the investigation frequently enough to assure that:

- The facilities used by the investigator continue to be acceptable for purposes of the study.
- The study protocol or investigational plan is being followed.
- Changes to the protocol have been approved by the IRB and/or reported to the sponsor and the IRB.
- Accurate, complete, and current records are being maintained.
- Accurate, complete, and timely reports are being made to the sponsor and IRB.
- The investigator is carrying out the agreed-upon activities and has not delegated them to other previously unspecified staff.

E. Review of Subject Records

A sponsor is responsible for assuring that the data submitted to FDA in support of the safety and effectiveness of a test article are accurate and complete. The most effective way to assure the accuracy of the data submitted to FDA is to review individual subject records and other supporting documents and compare those records with the reports prepared by the investigator for submission to the sponsor. Therefore, during a periodic visit, the monitor should compare a representative number of subject records and other supporting documents with the investigator's reports to determine that:

- The information recorded in the investigator's reports is complete, accurate, and legible.
- There are no omissions in the reports of specific data elements such as the administration to any subject of concomitant test articles or the development of an intercurrent illness.
- Missing visits or examinations are noted in the reports.
- Subjects failing to complete the study and the reason for each failure are noted in the reports.
- Informed consent has been documented in accordance with 21 CFR Parts 50 and 56.

F. Record of On-Site Visits

The monitor or the sponsor should maintain a record of the findings, conclusions, and action taken to correct deficiencies for each on-site visit to an investigator. Such a record may enable FDA to determine that a sponsor's obligations in monitoring the progress of a clinical investigation are being fulfilled. The record may include such elements as:

- The date of the visit.
- The name of the individual who conducted the visit.
- The name and address of the investigator visited.
- A statement of the findings, conclusions and any actions taken to correct any deficiencies noted during the visit.

GUIDANCE ON SIGNIFICANT AND NONSIGNIFICANT RISK DEVICE STUDIES

PREPARED BY:

OFFICE OF DEVICE EVALUATION
CENTER FOR DEVICES AND RADIOLOGICAL HEALTH

JUNE 1986

GUIDANCE ON SIGNIFICANT AND NONSIGNIFICANT RISK DEVICE STUDIES

An approved Investigational Device Exemption (IDE), or an exemption from the IDE regulation, permits clinical study of unapproved devices. The IDE regulation describes two types of device studies -- significant risk (SR) and nonsignificant risk (NSR).

The IDE regulation defines a SR device study as one that presents a potential for serious risk to the health, safety, or welfare of a subject; and, is an implant, is used in supporting or sustaining human life, is of substantial importance in diagnosing, curing, mitigating or treating disease, otherwise prevents impairment of human health, or otherwise presents a potential for serious risk to the health, safety, or welfare of a subject. A NSR investigation is one that does not pose a SR.

THE IMPORTANCE OF DISTINGUISHING BETWEEN SIGNIFICANT AND NONSIGNIFICANT RISK DEVICE STUDIES

NSR studies are subject to fewer regulatory controls than SR studies. If an investigator or a sponsor proposes the initiation of a NSR investigation to an Institutional Review Board (IRB), and if the IRB agrees that the device study is NSR and approves the study, the investigation may begin at that institution immediately, without FDA approval. If an IRB believes that a device study is a SR, the investigation may not begin until both the IRB and FDA approve the investigation. Also, there are fewer report and record keeping requirements for investigators and sponsors of nonsignificant risk device investigations. Thus, the effect of a SR/NSR decision is very important to sponsors and investigators. Nonetheless, the IRB should recognize the importance of their role in identifying NSR investigations that should be regulated less stringently than riskier studies.

THE IRB DECISION MAKING PROCESS

An IRB must make two separate decisions. First, is a proposed investigation SR or NSR. Second, is the investigation approvable or not. The criteria for the two decisions are different.

The NSR/SR Decision: An assessment of whether a device study presents a NSR is initially made by a sponsor. If a sponsor believes a study is NSR, the sponsor should provide an IRB with the study proposal, an explanation of why the study is NSR, and other supporting information, e.g., any reports of prior investigations. The sponsor should also tell the IRB if FDA or any other IRB has determined the study to be SR or NSR, and provide any other information requested by the IRB. The IRB may agree or disagree with the sponsor's initial NSR assessment. If an IRB agrees, the investigation may proceed without FDA approval. If an IRB disagrees, the study can only be conducted at that IRBs institution as a SR investigation, and the sponsor must notify FDA that a SR determination has been made (whether or not the sponsor ultimately conducts the study at that institution).

The sponsor and IRB should understand that a study with "a potential for serious risk" is one that presents a potential for serious harm. Thus, to determine if a study is a SR, an IRB must consider the nature of the harm that may result from use of the device. If a device being investigated might cause significant harm to any of the subjects, the study should be considered SR. Also, if the subject must undergo a procedure as part of the investigational study, e.g., a surgical procedure, the IRB should consider the potential harm that could be caused by the procedure as well as the potential harm caused by the device. Those investigations where the potential harm to subjects could be life threatening, could result in permanent impairment of a body function, or permanent damage to body structure, or could necessitate medical or surgical intervention to preclude permanent impairment of a body function or permanent damage to body structure, are included among those studies that are SR. Some examples follow:

- o The study of a pacemaker that is a modification of a commercially-available pacemaker poses a SR because the use of any pacemaker presents a potential for serious harm to the subjects. This is true even though the modified pacemaker may pose less risk, or only slightly greater risk, in comparison to the commercially-available model. The degree of possibly reduced or increased risk associated with the investigational pacemaker should only be considered (in relation to possible decreased or increased benefits) when assessing the approvability of the study.

- o The study of an extended wear contact lens is considered SR because wearing the lens continuously for 30 days presents a potential for injuries not normally seen with daily wear lenses, which are considered NSR.

While the IRB normally serves as FDA's surrogate with respect to review and approval of NSR studies, the ultimate decision in determining if a device study is SR or NSR is FDA's. On some occasions, FDA may overrule an IRB's decision that a device study presents NSR or SR. When FDA overrules an IRBs NSR determination, an IDE application must be submitted to FDA. On the other hand, when FDA considers the device study to be NSR, FDA may return an IDE application to the sponsor and the IRB must then determine if it wants the study to take place in its institution as a NSR investigation.

The Decision to Approve or Disapprove: Once a decision on the degree of risk has been reached, the IRB should consider whether the study should be approved or not. Generally, full IRB review is required when reviewing both SR and NSR studies. Some NSR studies, however, may also be considered minimal risk, i.e., the risk is no greater than that encountered in daily activities, and the IRB may choose to review those under their expedited review procedures. Minor changes in already approved studies may also be reviewed through the expedited review procedure.

The criteria for deciding if either a SR or NSR study should be approved are the same as those used to evaluate research involving any FDA regulated product. The IRB should determine that risks to subjects are minimized, risks to subjects are reasonable in relation to anticipated benefits and knowledge to be gained, subject selection is equitable, informed consent materials and procedures are adequate, and there are acceptable provisions for monitoring the study and protecting patient information. To determine that the risks to the subject are reasonable in relation to the anticipated benefits, the risks and benefits for the investigation should be compared to the risks and benefits of alternative devices or procedures. This differs from the judgment about whether a study poses SR or NSR. That decision is based upon the seriousness of the nature of the harm that may result from the use of the device.

EXAMPLES OF NSR/SR STUDIES

The examples below are provided to assist sponsors and IRBs in making SR/NSR determinations. They are not exhaustive. Remember that a risk determination is based on the proposed use of a device in an investigation, not on the device alone. In the examples listed below, where there are no specific uses described, the Center believes that all reasonable uses of the device would be included in the risk category where the device is placed. The Center anticipates periodically revising and updating this guidance, including the list of examples of SR and NSR devices.

Nonsignificant Risk Device Studies:

Biostimulation Lasers for treatment of pain
Caries Removal Solution
Daily Wear Contact Lenses and Associated Cleaners & Solutions
Dental Filling Materials, Cushions or Pads made from traditional materials and designs
Denture Repair Kits and Realiners
Gynecologic Laparoscope and Accessories at power levels established prior to May 28, 1976 (excluding use in female sterilization)
Externally Worn Monitor for Insulin Reactions
Jaundice Monitor for Infants
Magnetic Resonance Imaging (MRI) Devices within specified physical parameters
Menstrual Pads
Menstrual Tampons of "old" materials (used prior to May 28, 1976)
Nonimplantable Male Reproductive Aids
Ob/Gyn Diagnostic Ultrasound (within specified parameters)
Transcutaneous Electric Nerve Stimulation (TENS) Devices for treatment of pain
Wound Dressings, excluding absorbable hemostatic devices and dressings

Significant Risk Device Studies:

GENERAL MEDICAL USE

Catheters: Cardiology - diagnostic, treatment, transluminal coronary angiolplasty, intra-aortic balloon with control system
Gastroenterology and Urology - biliary and urologic
General Hospital - long-term percutaneous, implanted, subcutaneous and intravascular
Neurology - cerebrovascular, occlusion balloon
Collagen Implant Material for use in ear, nose and throat, orthopedics and plastic surgery
Lasers for use in Ob/Gyn, cardiology, gastroenterology, urology, pulmonarnesthesia Apparatus
Gas Machines for anesthesia or analgesia
High Frequency Jet Ventilators greater than 150 BPM

CARDIOVASCULAR

Arterial Embolization Device
Artificial Heart, permanent implant and short term use
Cardiac Bypass Systems: oxygenator, cardiopulmonary blood pump, ventricular assist devices
Cardiac Pacemaker/Pulse Generator: implantable, external transcutaneous, antitachycardia, esophageal

Cardiovascular/Intravascular Filters
Coronary Artery Retroperfusion System
DC-Defibrillators
Implantable Cardioverters
Laser Coronary Angioplasty Device
Pacemaker Programmer
Percutaneous Conduction Tissue Ablation Electrode
Replacement Heart Valve
Vascular and Arterial Graft Prostheses

DENTAL

Endosseous Implant

EAR, NOSE AND THROAT

Cochlear Implant
Total Ossicular Prosthesis Replacement

GASTROENTEROLOGY AND UROLOGY

Anastomosis Device
Endoscope and/or Accessories
Extracorporeal Hyperthermia System
Extracorporeal Photophersis System
Extracorporeal Shock-Wave lithotriptor
Kidney Perfusion System
Mechanical/Hydraulic Impotence and Incontinence Devices
Implantable Penile Prosthesis
Peritoneal Shunt

GENERAL AND PLASTIC SURGERY

Absorbable Hemostatic Agents
Artificial Skin
Injectable Silicone
Implantable Prostheses: chin, nose, cheek, ear
Sutures

GENERAL HOSPITAL

Infusion Pumps: implanted and closed-loop, depending on infused drug
Implantable Vascular Access devices

NEUROLOGY

Hydrocephalus Shunts
Implanted Intracerebral/Subcortical Stimulator
Implanted Intracranial Pressure Monitor
Implanted Spinal Cord and Nerve Stimulators and Electrodes

OBSTETRICS AND GYNECOLOGY

Cervical Dilator
Chorionic Villus Sampling Catheter, phase II (pregnancy continued to term)
Contraceptive Devices: tubal occlusion, cervical cap, diaphragm, intrauterine device (IUD) and introducer, and sponge

OPHTHALMICS

Extended Wear Contact Lens
Intraocular Lens (investigations subject to 21 CFR 813)
Eye Valve Implant
Retinal Reattachment Systems: sulfur hexafluoride, silicone oil, tacks, perfluoropropane

ORTHOPEDICS

Implantable Prostheses: ligament, tendon, hip, knee, finger
Bone Growth Stimulator
Calcium Tri-Phosphate/Hydroxyapatite Ceramics
Xenografts

RADIOLOGY

Hyperthermia Systems and Applicators

Your comments on the guidance and list of examples, and suggestions for additional examples, are welcome and should be sent to:

Nancy Teague
Director, IDE Staff, HFZ-403
Center for Devices and Radiological Health
5600 Fishers Lane
Rockville, Maryland 20857
(301) 427-8162

SUGGESTED FORMAT FOR IDE PROGRESS REPORTS

I. The Basics

- IDE Number
- Device name and indication for use
- Sponsor's name, address and phone number
- Contact person

II. Study Progress

(Data from beginning of the study should be reported, unless otherwise indicated.)

- Brief summary of study progress in relation to investigational plan
- Number of investigators/investigational sites (attach list of investigators)
- Number of subjects enrolled (by indication or model)
- Number of devices shipped
- Brief summary of results
- Summary of anticipated and unanticipated adverse effects
- Description of any deviations from the investigational plan by investigators (since last progress report)

III. Risk Analysis

- Summary of any new adverse information (since last progress report) that may affect the risk analysis; this includes preclinical data, animal studies, foreign data, clinical studies, etc.
- Reprints of any articles published from data collected from this study
- New risk analysis, if necessary, based on new information and on study progress

IV. Other Changes

- Summary of any changes in manufacturing practices and quality control (including changes not reported in a supplemental application)
- Summary of all changes in investigational plan not required to be submitted in a supplemental application

V. Future Plans

- Progress toward product approval, with projected date of PMA or 510(k) submission
- Any plans to change investigation, e.g., to expand study size or indications, to discontinue portions of the investigation or to change manufacturing practices (NOTE: Actual proposals for change should be made in a separate supplemental application).

8 PREMARKET APPROVAL

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INTRODUCTION

Under Section 515 of the Federal Food, Drug, and Cosmetic Act (the Act), all devices placed into Class III are subject to premarket approval requirements. The Amendments provide that a Class III device is "purported or represented to be for a use in supporting or sustaining human life or for a use which is of substantial importance in preventing impairment of human health, or presents a potential unreasonable risk of illness or injury." In addition, such a device cannot be classified into Class I because insufficient information exists to determine that general controls are sufficient to provide reasonable assurance of the safety and effectiveness of the device. It cannot be classified as a Class II device because insufficient information exists for the establishment of a performance standard to provide reasonable assurance of safety and effectiveness. Premarket approval is a process of scientific and regulatory review to insure the safety and effectiveness of Class III devices.

An approved Premarket Approval Application (PMA), like an approved New Drug Application (NDA), is, in effect, a private license granted to the applicant for marketing a particular medical device. A Class III device that fails to meet PMA requirements is considered to be adulterated under Section 501(f) of the Act and cannot be marketed. Premarket approval requirements apply differently to preamendments devices, postamendments devices, and Class III transitional devices.

A preamendments device is one that was in commercial distribution before May 28, 1976, the enactment date of the Medical Device Amendments. Manufacturers of Class III preamendments devices are not required to submit a PMA until 30 months after the promulgation of a final classification regulation or until 90 days after the publication of a final regulation requiring the submission of a PMA, whichever period is later. FDA may allow more than 90 days after promulgation of a final rule for submission of a PMA.

A postamendments device is one that was first distributed commercially on or after May 28, 1976. Postamendments devices that FDA determines are substantially equivalent to preamendments Class III devices are subject to the same requirements as the preamendments devices. FDA determines substantial equivalence after reviewing an applicant's premarket notification submitted in accordance with Section 510(k) of the Act. Postamendments devices determined by FDA to be not substantially equivalent to either preamendments devices or postamendments devices classified into Class I or II are "new" devices and fall automatically into Class III. Before such devices can be marketed, they must have an approved premarket approval application or be reclassified into Class I or Class II.

Class III transitional devices and "new" devices (described in the paragraph above) are automatically classified into Class III by statute and require premarket approval by FDA before they may be commercially distributed. Applicants may either submit a PMA or a Product Development Protocol (PDP), or they may petition FDA to reclassify the devices into Class I or Class II. Clinical studies in support of a PMA, a PDP, or a reclassification petition are subject to the Investigational Device Exemption (IDE) regulation. For further details on these regulations, refer to 21 CFR 812 for general devices or 21 CFR 813 for intraocular lenses as well as the chapter on "Investigational Device Exemptions."

The following is not an all-inclusive list of transitional devices for which premarket approval is required. These devices were formerly regulated by FDA as new drugs or antibiotic drugs [42 FR 63473 (December 16, 1977) and 45 FR 58964 (September 5, 1980)].

- Absorbable hemostatic devices and dressings
- Biological in vitro diagnostic products used as aids for the detection and management of cancer in humans (only those that include the biologically derived substances CEA, AFP, TAA, or TPA)
- Bone cements
- Bone heterographs
- Cervical smear processing devices
- Desiccant and lubricant powders for surgical gloves
- Gases used within eye to place pressure on detached retina
- Gonorrhea diagnostic products (indirect serological test)
- Injectable silicone
- Injectable teflon
- Intraocular lenses
- Pregnancy test kits (non-immunological test)
- Soft contact lenses, cleaning (sterilizing) agents, and wetting agents
- Surgical sutures (absorbable and nonabsorbable)
- Tissue adhesives
- Triphosphate granules for dental bone repair
- Vascular grafts of animal origin

* Some types of surgical sutures have been reclassified to Class II.

THE PMA REVIEW PROCESS

The review of a premarket approval application is a 4-step review process consisting of:

- administrative and limited scientific review by FDA staff to determine completeness (filing review);

- in-depth scientific and regulatory review by appropriate FDA scientific and compliance personnel (in-depth review);
- review and recommendation by the appropriate advisory committee (panel review); and
- final deliberations, documentation, and notification of the FDA approval decision.

During the administrative and limited scientific review, FDA determines whether a PMA includes the type of information required by the Act and the PMA procedural regulations (21 CFR 814) and is suitable for filing. The filing of a PMA application means that FDA has made a threshold determination that the application is sufficiently complete to permit a substantive review. If the information or data are presented unclearly or incompletely or are not capable of withstanding rigorous scientific review, FDA may consider the PMA incomplete and not file it. The filing date is the date that FDA receives a PMA which it subsequently considers to be suitable for filing, and the 180-day review period provided by the Act begins on this filing date.

A PMA accepted for filing undergoes an in-depth scientific review by FDA personnel and an advisory committee representing the appropriate medical field. FDA then notifies the PMA applicant of any deficiencies. Within the 180-day review period, FDA will send the applicant an approval order under 814.44(d), an approvable letter under 814.44(e), a not approvable letter under 814.44(f), or an order denying approval under 814.45.

FDA will notify the applicant by letter of its decision, and a FEDERAL REGISTER notice will announce the decision and the availability of a summary of the safety and effectiveness data on which the decision is based. It also provides the applicant and other interested persons an opportunity for administrative review of the FDA approval or denial action.

The PMA staff has issued more recent materials on the submission of PMA documents. These include the Premarket Approval (PMA) Manual and Standard Conditions of Approval.

This chapter includes pertinent portions of the Premarket Approval (PMA) Manual and the Standard Conditions of Approval applicable to all approved original and supplemental PMAs. Copies of the PMA Manual are available from:

Division of Small Manufacturers Assistance, HFZ-220
Food and Drug Administration
5600 Fishers Lane
Rockville, Maryland 20857

CONTENT OF APPLICATIONS

Section 515(c)(1) of the Act specifies the following:

> (c)(1) Any person may file with the Secretary an application for premarket approval for a Class III device. Such an application for a device shall contain--
>
> (A) full reports of all information, published or known to or which should reasonably be known to the applicant, concerning investigations which have been made to show whether or not such device is safe and effective;

(B) a full statement of the components, ingredients, and properties and of the principle or principles of operation, of such device;

(C) a full description of the methods used in, and the facilities and controls used for, the manufacture, processing, and, when relevant, packing and installation of, such device;

(D) an identifying reference to any performance standard under Section 514 which would be applicable to any aspect of such device if it were a Class II device, and either adequate information to show that such aspect of such device fully meets such performance standard or adequate information to justify any deviation from such standards;

(E) such samples of such device and of components thereof as the Secretary may reasonably require, except that where the submission of such samples is impracticable or unduly burdensome, the requirement of this subparagraph may be met by the submission of complete information concerning the location of one or more such devices readily available for examination and testing;

(F) specimens of the labeling proposed to be used for such device; and

(G) such other information relevant to the subject matter of the application as the Secretary, with the concurrence of the appropriate panel under Section 513, may require.

STANDARD CONDITIONS OF APPROVAL

The "Conditions of Approval" are the standard postapproval conditions applicable to all original PMAs and PMA supplements. Additional specific conditions may be required for implanted devices. Applicants should carefully read the conditions of approval enclosed with the FDA approval letter. The following is an example of a "Conditions of Approval" letter.

Approved Labeling

As soon as possible, and before commercial distribution of your device, submit two copies of an amendment to this PMA submission with copies of all approved labeling in final printed form to the PMA Document Mail Center (HFZ-401), Center for Devices and Radiological Health, Food and Drug Administration, 5600 Fishers Lane, Rockville, Maryland 20857.

Advertisement

No advertisement and other descriptive printed material issued by the applicant or private label distributor with respect to this device shall recommend or imply that the device may be used for any use that is not included in the FDA approved labeling for the device. If FDA has restricted the sale, distribution and use of the device to prescription use in accordance with 801.109 within the meaning of Section 520(e) of the Act under the authority of Section 515(d)(1)(B)(ii) of the Act, all advertisements and other descriptive printed material issued by the applicant or distributor with respect to the device shall include a brief statement of the intended uses of the device and relevant warnings, precautions, side effects and contraindications.

Premarket Approval Application (PMA) Supplement

Before making any change affecting the safety or effectiveness of the device, submit a PMA supplement for review and approval by FDA unless the change is of a type for which a "Special PMA Supplement--Changes Being Effected" is permitted under 814.39(d) or for which FDA has advised in an advisory opinion or in correspondence in accordance with 814.39(e) that an alternate submission is permitted. A PMA supplement or alternate submission shall comply with applicable requirements under 814.39 of the final rule for Premarket Approval of Medical Devices (51 FR 26342) published in the FEDERAL REGISTER of July 22, 1986.

Postapproval Reports

Continued approval of this PMA is contingent upon the submission of postapproval reports required under 814.84 at intervals of 1 year from the date of approval of the original PMA. Postapproval reports for supplements approved under the original PMA, if applicable, are to be included in the next and subsequent annual reports for the original PMA unless specified otherwise in the approval order for the PMA supplement. Two copies identified as "Annual Report" and bearing the applicable PMA reference number are to be submitted to the PMA Document Mail Center (HFZ-401), Center for Devices and Radiological Health, Food and Drug Administration, 5600 Fishers Lane, Rockville, Maryland 20857. The postapproval report shall indicate the beginning and ending date of the period covered by the report and shall include the following information required by 814.84:

(1) Identification of changes described in 814.39(a) and changes required to be reported to FDA under 814.39(b).

(2) Bibliography and summary of the following information not previously submitted as part of the PMA and that is known to or reasonably should be known to the applicant:

(a) unpublished reports of data from any clinical investigations or nonclinical laboratory studies involving the device or related devices ("related" devices include devices which are the same or substantially similar to the applicant's device); and

(b) reports in the scientific literature concerning the device.

If, after reviewing the bibliography and summary, FDA concludes that FDA review of one or more of the above reports is required, the applicant shall submit two copies of each identified report when so notified by FDA.

Adverse Reaction and Device Defect Reporting

As provided by 814.82(a)(9), FDA has determined that in order to provide continued reasonable assurance of the safety and effectiveness of the device, the applicant shall submit three copies of a written report identified as an "Adverse Reaction Report" or "Device Defect Report," as applicable, to the PMA Document Mail Center (HFZ-401), Center for Devices and Radiological Health, Food and Drug Administration, 5600 Fishers Lane, Rockville, Maryland 20857 within ten days after the applicant receives or has knowledge of information concerning:

(1) A mixup of the device or its labeling with another article;

(2) Any adverse reaction, side effect, injury, toxicity, or sensitivity reaction that is attributable to the device which:

(a) has not been addressed by the device's labeling; or

(b) has been addressed by the device's labeling, but is occurring with unexpected severity or frequency;

(3) Any significant chemical, physical or other change or deterioration in the device or any failure of the device to meet the specifications established in the approved PMA that could not cause or contribute to death or serious injury but are not correctable by adjustments or other maintenance procedures described in the approved labeling. The report shall include a discussion of the applicant's assessment of the change, deterioration or failure and any proposed or implemented corrective action by the applicant. When such events are correctable by adjustments or other maintenance procedures described in the approved labeling, all such events known to the applicant shall be included in the Annual Report described under "Postapproval Reports" above unless specified otherwise in the conditions of approval to this PMA. This postapproval report shall appropriately categorize these events and include the number of reported and otherwise known instances of each category during the reporting period. Additional information regarding the events discussed above shall be submitted by the applicant when determined by FDA to be necessary to provide continued reasonable assurance of the safety and effectiveness of the device for its intended use.

Reporting under the Medical Device Reporting (MDR) Regulation

The Medical Device Reporting (MDR) Regulation became effective on December 13, 1984, and requires that all manufacturers and importers of medical devices, including in vitro diagnostic devices, report to FDA whenever they receive or otherwise become aware of information that reasonably suggests that one of its marketed devices (1) may have caused or contributed to a death or serious injury, or (2) has malfunctioned and that the device or any other device marketed by the manufacturer or importer would be likely to cause or contribute to a death or serious injury if the malfunction were to reoccur.

The "Conditions of Approval" accompanying PMA approval orders may require that the same events subject to reporting under the MDR regulation must also be included in periodic reports to the PMA. FDA has determined that such duplicative reporting is unnecessary. Whenever an event involving a device is subject to reporting under both the MDR regulation and the "Conditions of Approval" for this PMA, you shall submit the appropriate reports required by the MDR regulation and identified with the PMA reference number to the following office:

Device Monitoring Branch (HFZ-343)
Center for Devices and Radiological Health
Food and Drug Administration
5600 Fishers Lane
Rockville, Maryland 20857
Telephone: (301) 427-7500

Events included in periodic reports to the PMA that have also been reported under the MDR regulation must be so identified in the periodic report to the PMA to prevent duplicative entry into FDA information systems.

Copies of the MDR regulation and an FDA publication entitled, "An Overview of the Medical Device Reporting Regulation," are available by written request to the above address or by telephoning (301) 427-8100.

(End of example of "Conditions of Approval" letter.)

OVERVIEW OF THE PMA PROCEDURAL REGULATION

Below is an outline of the PMA regulation followed by an overview with section numbers identified in parentheses.

PART 814 - PREMARKET APPROVAL OF MEDICAL DEVICES

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AUTHORITY: Secs. 501-503, 510, 513-520, 701(a), 702, 703, 704, 705, 706, 708, and 801, 52 Stat. 1049-1058 as amended, 67 Stat. 477 as amended, 74 Stat. 399-407 as amended, 76 Stat. 794-795 as amended, 90 Stat. 540-574, 582-583 (21 U.S.C. 351, 352, 353, 360, 360c-360j, 371(a), 373, 374, 375, 379, 381); Pub. L. 90-23, 81 Stat. 54-56 as amended by 88 Stat. 1561-1565 (5 U.S.C. 552); 21 CFR 5.11.

Subpart A - General

Scope (21 CFR 814.1)

The regulation implements Section 515 of the Act by providing procedures for premarket approval of medical devices intended for human use. It applies to any Class III medical device, unless exempt under Section 520(g) (investigational use) of the Act, that:

- was not on the market before May 28, 1976, and is not substantially equivalent to a device on the market before May 28, 1976, or to a device first marketed on or after that date, which has been classified into Class I (general controls) or Class II (performance standards); or
- is required by a regulation issued under Section 515(b) of the Act to have an approved Premarket Approval Application (PMA) or a declared completed Product Development Protocol (PDP); or
- was regulated by FDA as a new drug or an antibiotic drug before May 28, 1976, and therefore is governed by Section 520(l) of the Act (transitional devices).

The regulation also amends the conditions to approval for any PMA previously approved. Any condition to approval for an approved PMA that is inconsistent with the regulation is revoked, while those conditions to approval that are consistent with this regulation remain in effect.

Purpose (21 CFR 814.2)

The purpose of the regulation is to establish an efficient and thorough device review process to:

- facilitate the approval of PMAs for devices that have been shown to be safe and effective and that otherwise meet the statutory criteria for approval; and
- ensure the disapproval of PMAs for devices that have not been shown to be safe and effective or that do not otherwise meet the statutory criteria for approval.

Definitions (21 CFR 814.3)

The following definitions are used in the PMA regulation:

- "Act" means the Federal Food, Drug, and Cosmetic Act [Sections 201-902, 52 Stat. 1040 et seq., as amended (21 USC 321-392)].
- "FDA" means the Food and Drug Administration.
- "IDE" means an approved or considered approved Investigational Device Exemption under Section 520(g) of the Act and Parts 812 and 813.
- "Master file" means a reference source that a person submits to FDA. A master file may contain detailed information on a specific manufacturing facility, process, methodology, or component used in the manufacture, processing, or packaging of a medical device.

- "PMA" means any Premarket Approval Application for a Class III medical device, including all information submitted with or incorporated by reference. "PMA" includes a new drug application for a device under Section 520(l) of the Act.

- "PMA amendment" means information an applicant submits to FDA to modify a pending PMA or a pending PMA supplement.

- "PMA supplement" means a supplemental application to an approved PMA for approval of a change or modification in a Class III medical device, including all information submitted with or incorporated by reference.

- "Person" includes any individual, partnership, corporation, association, scientific or academic establishment, government agency or organizational unit, or any other legal entity.

- "Statement of material fact" means a representation that tends to show that the safety or effectiveness of a device is more probable that it would be in the absence of such a representation. A false affirmation or silence or an omission that would lead a reasonable person to draw a particular conclusion as to the safety or effectiveness of a device also may be a false statement of material fact, even if the statement was not intended by the person making it to be misleading or to have any probative effect.

- "30-day PMA supplement" means a supplemental application to an approved PMA in accordance with 21 CFR 814.39(e).

Confidentiality (21 CFR 814.9)

A "PMA file" includes all data and information submitted with or incorporated by reference into the PMA, any IDE incorporated into the PMA, any PMA supplement, any report (814.82 and 814.84), any master file, or any other related submission. Any record in the PMA file will be available for public disclosure in accordance with the provisions of this section and Part 20 (Public Information). The confidentiality of information in a color additive petition submitted as part of a PMA is governed by 71.15.

The existence of a PMA file may not be disclosed by FDA before the agency has approved or disapproved the PMA, unless it has been previously disclosed publicly or acknowledged. If the existence of a PMA file has not been publicly disclosed or acknowledged, data or information in the PMA file are not available for public disclosure. Even if the existence of a PMA has been publicly disclosed or acknowledged before FDA has approved or disapproved the PMA, data or information contained in the PMA file still are not available for public disclosure before FDA has issued its decision. FDA may, however, disclose a summary of portions of the safety and effectiveness data before issuing an approval decision, if such disclosure is relevant to public consideration of a specific pending issue.

After FDA has approved or disapproved a PMA, the agency will make known to the public the existence of the PMA and a detailed summary of the safety and effectiveness information on which the decision is based. The following data and information in the PMA file are then immediately available for public disclosure:

- all safety and effectiveness data and information previously disclosed to the public as defined in 20.81;

- any protocol for a test or study unless it constitutes a trade secret or confidential commercial or financial information under 20.61;

- any adverse reaction report, product experience report, consumer complaint, and other similar data and information after deletion of any information that constitutes trade secret or confidential commercial or financial information under 20.61; and any personnel, medical, and similar information whose disclosure would constitute a clearly unwarranted invasion of personal privacy under 20.63; however, FDA will disclose to a patient who requests a report all of the information in the report concerning that patient;

- a list of components previously disclosed to the public (20.81);

- an assay or other analytical method, unless it does not serve any regulatory purpose and is exempt under 20.61 as trade secret or confidential commercial or financial information; and

- all correspondence and written summaries of oral discussions relating to the PMA file in accordance with 20.103 and 20.104.

All safety and effectiveness data and other information that was not previously disclosed to the public and that is not a trade secret or confidential commercial or financial information (20.61) are available for public disclosure in the following instances:

- The PMA has been abandoned. FDA will consider a PMA abandoned if: (a) the applicant fails to respond to a request for additional information within 180 days after the date FDA issues the request or other circumstances indicate that further work is not being undertaken with respect to it; and (b) the applicant fails to communicate with FDA within seven days after the date on which FDA notifies the applicant that the PMA appears to have been abandoned;

- FDA has issued an order denying approval of the PMA, and all legal appeals have been exhausted;

- FDA has withdrawn approval of the PMA, and all legal appeals have been exhausted;

- The device has been reclassified to Class I or Class II;

- The device has been found to be substantially equivalent to a Class I or Class II device; or

- The PMA is considered voluntarily withdrawn under 814.44(g).

The following data and information in a PMA file are not available for public disclosure unless previously disclosed or they relate to a device for which a PMA has been abandoned and it no longer represents a trade secret or is confidential commercial or financial information:

- manufacturing methods or processes including quality control procedures;

- production, sales, distribution, and similar data and information, except compilation of such information that does not reveal data or information which are not available for public disclosure; and o quantitative or semiquantitative formulas.

Research conducted outside the United States (21 CFR 814.15)

A study conducted under an Investigational Device Exemption (IDE) outside the United States and submitted in support of a PMA must comply with Investigational Device Exemptions (812). A study conducted outside the United States which was not conducted under an IDE must comply with one of the following:

o Research begun on or after effective date. FDA will accept studies which have been conducted outside the United States and begun on or after November 19, 1986, if the data constitute valid scientific evidence (860.7) and the investigator has conducted the studies in conformance with the "Declaration of Helsinki" or the laws and regulations of the country in which the research was conducted, whichever offers greater protection to the human subjects. If the standards of the country are used, the applicant must state in detail any differences between those standards and the "Declaration of Helsinki" and explain why the national standards offer greater protection to the human subjects.

o Research begun before effective date. FDA will accept studies which have been conducted outside the United States and begun before November 19, 1986, if the agency is satisfied that the data constitute valid scientific evidence (860.7) and that the rights, safety, and welfare of human subjects have not been violated.

A PMA based solely on foreign clinical data and otherwise meeting the criteria for approval under this part may be approved if:

o the foreign data are applicable to the United States population and medical practice:

o the studies have been performed by clinical investigators of recognized competence: and

o the data may be considered valid without the need for an on-site inspection by FDA or, if FDA considers such an inspection to be necessary, FDA can validate the data through an on-site inspection or other appropriate means.

Applicants who seek approval based solely on foreign data are encouraged to meet with FDA officials in a presubmission meeting.

Service of orders (21 CFR 814.17)

Any FDA orders (approval, denial, etc.) will be delivered by a designated officer or employee of FDA or by registered mail to the PMA applicant or its designated agent.

Product development protocol (PDP) (21 CFR 814.19)

FDA will consider a Class III device for which FDA has declared that a Product Development Protocol has been completed, to have an approved PMA.

Subpart B - Premarket Approval Application

Application (21 CFR 814.20)

A PMA must be signed by the applicant or an authorized representative. If the applicant does not reside or have a place of business within the United States. the PMA must be countersigned by an authorized representative who does. The applicant must also submit the representative's name and address.

Unless an omission is justified by the applicant [814.20(d)]. a PMA must include all of the following:

1. The name and address of the applicant.

2. A table of contents that specifies the volume and page number for each item referred to in the table.

   The PMA must include separate sections on nonclinical laboratory studies and on clinical investigations involving human subjects. Six copies of the PMA are required. each bound in one or more numbered volumes of reasonable size. To facilitate review by the advisory committee(s). additional copies may be requested by FDA.

   Trade secret or confidential commercial or financial information must be included in all copies of the PMA. The applicant must identify in at least one copy any information that they believe to be trade secret or confidential commercial or financial information.

3. A summary section in sufficient detail to provide a general understanding of the data and information in the application. (Note: The summary section would contain brief statements of major points found elsewhere in the PMA and would typically be 10 to 15 pages in length.)

   The summary section must contain the following information:

   o Indications for use. Give a general description of the disease or condition that the device will diagnose. treat. prevent. cure. or mitigate and include a description of the patient population for which the device is intended.

   o Device description. Explain how the device functions. the basic scientific concepts that form the basis for the device. and the significant physical and performance characteristics of the device. A brief description of the manufacturing process should be included if it will significantly enhance the reader's understanding of the device. The generic name of the device as well as any proprietary name or trade name should be included.

   o Alternative practices and procedures. Describe any alternative practices or procedures for diagnosing. treating. preventing. curing. or mitigating the disease or condition for which the device is intended.

- Marketing history. Give a brief description of the foreign and United States marketing history, if any, of the device known to the applicant. At a minimum include a list of all countries in which the device has been marketed and a list of all countries in which the device has been withdrawn from marketing for any reason related to the safety or effectiveness of the device. (Note: It would be appropriate to include the countries in which it has been marketed and dates of introduction, information about the quantity of product distributed in each country, a brief description of any experience reporting mechanism, a summary of any adverse experiences reported, and information about any withdrawals for any reason related to the safety or effectiveness, i.e., withdrawals because of poor sales or physician disfavor should not be included.) The description must include the history of the marketing of the device by the applicant and, if known, the history of the marketing of the device by any other person.

- Summary of studies. This section must contain: (1) an abstract of any other data, information, or report described in the PMA under 814.20(b)(8)(ii) of this section; and (2) a summary of the results of the clinical investigations and nonclinical laboratory studies conducted by or for the applicant.

  The summary must include a description of the objective of each study or hypothesis tested, a brief discussion of how the data were collected and analyzed, and a brief description of the findings and conclusions, whether positive, negative or inconclusive. This section must include: (a) a summary of the nonclinical laboratory studies submitted in the application; and (b) a summary of the clinical investigations involving human subjects including a discussion of subject selection and exclusion criteria, study population demographics, study period, safety and effectiveness data, adverse reactions and complications, patient discontinuation, device failures and replacements, results of statistical analyses of the clinical investigations, contraindications and precautions for use of the device, and other information from the clinical investigations as appropriate. Any investigation conducted under an IDE must be identified.

- Conclusions drawn from the studies. Discuss how the data and information in the application constitute valid scientific evidence within the meaning of 860.7 (Determination of Safety and Effectiveness) and provide reasonable assurance that the device is safe and effective for its intended use. A concluding discussion must present benefit and risk considerations related to the device, any adverse effects of the device on health, and any proposed additional studies or surveillance that the applicant intends to conduct following approval of the PMA.

(Note: The applicant's summary section should objectively link the medical claim(s) for the device to the hypotheses tested and conclusions drawn from the findings of all studies and investigations. Biased presentation of the study data and inclusion of promotional claims are to be avoided. When preparing the summary section, the applicant should be able to detect and correct any accountability discrepancies, incomplete reporting and study design deficiencies which an in-depth scientific review would discover. A properly developed summary section by the applicant can serve as the basis for FDA's Summary of Safety and Effectiveness Data and will facilitate the FDA and panel review process. A full and explicit account of the clinical investigations and supporting data are needed to meet the legal requirements imposed by the Act. For a more detailed discussion of how to design, document, and present a clinical investigation to demonstrate safety and effectiveness, see "Guidance for Clinical Investigations for a PMA" available as part of the PMA Manual.)

4. A complete description of:

   - o the device, including pictorial representations;
   - o each of the functional components or ingredients of the device if the device consists of more than one physical component or ingredient;
   - o the properties of the device relevant to the diagnosis, treatment, prevention, cure, or mitigation of a disease or condition;
   - o the principles of operation of the device; and
   - o the methods, facilities, and controls used in the manufacture, processing, packing, storage, and where appropriate, installation of the device in sufficient detail so that a person generally familiar with current good manufacturing practices can make a knowledgeable judgement about the quality control used in the manufacture of the device.

   (Note: If complete manufacturing information is not available at the time the PMA is submitted, its temporary omission may be justified as provided in 814.20(d). Refer to Item 31 in the preamble for further information.)

5. Reference to any (a) performance standard promulgated under Section 514 of the Act or the Radiation Control for Health and Safety Act of 1968 (42 USC 263b et seq.) in effect or proposed at the time of the PMA submission and to any (b) voluntary standard that is specifically applicable to any aspect of the safety or effectiveness of the device [and was developed in accord with the FDA policy statement on standards development published in the FEDERAL REGISTER of October 23, 1985 (50 FR 43081)]. The applicant must provide adequate information to demonstrate how the device meets, or justify any deviation from, any of the above mandatory performance standards and explain any deviation from a voluntary standard.

   (Note: Upon request, FDA will provide a complete list of voluntary standards meeting the FDA policy statement that are applicable to the PMA applicant's device.)

6. Technical sections containing data and information in sufficient detail to permit FDA to determine whether to approve or disapprove the application.

   These sections and their contents are as follows:

   - o A section containing results of the nonclinical laboratory studies with the device. This section includes information on microbiology, toxicology, immunology, biocompatability, stress, wear, shelf life, and other laboratory or animal tests as appropriate. Information on nonclinical laboratory studies must include a statement that each such study was conducted in compliance with Part 58 (Good Laboratory Practice for Nonclinical Laboratory Studies); or, if the study was not conducted in compliance with such regulations, a brief statement of the reason for the noncompliance.

- A section containing results of the clinical investigations involving human subjects. This section includes study protocols, number of investigators and subjects per investigator, subject selection and exclusion criteria, study population demographics, study period, safety and effectiveness data, adverse reactions and complications, patient discontinuation, patient complaints, device failures and replacements, tabulations of data from all individual subject report forms and copies of such forms for each subject who died during a clinical investigation or who did not complete the investigation, results of statistical analyses of the clinical investigations, contraindications and precautions for use of the device, and any other appropriate information from the clinical investigations. Information on clinical investigations involving human subjects must include the following:

  (a) A statement with respect to each study that it either was conducted in compliance with the Institutional Review Board (IRB) regulations in Part 56, or was not subject to the regulations under 56.104 or 56.105, and that it was conducted in compliance with the Informed Consent regulations in Part 50. If the study was not conducted in compliance with those regulations, give a brief statement of the reason for the noncompliance.

  (b) A statement that each study was conducted in compliance with Part 812 (Investigational Device Exemptions) or Part 813 (Investigational Exemptions for Intraocular Lenses) concerning sponsors of clinical investigations and clinical investigators. If the study was not conducted in compliance with those regulations, give a brief statement of the reason for the noncompliance.

7. For a PMA supported solely by data from one investigator, a justification showing why data and other information from a single investigator are sufficient to demonstrate the safety and effectiveness of the device and to ensure reproducibility of test results.

8. A bibliography of all published reports not already submitted, whether adverse or supportive, that are known to or should reasonably be known to the applicant and that concern the safety or effectiveness of the device.

   An identification, discussion, and analysis of any other data, information, or report relevant to an evaluation of the safety and effectiveness of the device that are known to or should reasonably be known to the applicant from any source, foreign or domestic. This includes information from investigations other than those proposed in the application and from commercial marketing experience.

   Copies of such published reports or unpublished information in the possession of (or reasonably obtainable by) the applicant, if an FDA advisory committee or FDA requests.

9. One or more samples of the device and its components, if requested by FDA. If it is impractical to submit a requested sample of the device, the applicant should name the location at which FDA may examine and test one or more devices.

10. Copies of all proposed labeling for the device. Such labeling may include, for example, instructions for installation and any information, literature, or advertising that constitutes labeling under Section 201(m) of the Act. (Note: Any advertising devised by applicant that does not constitute labeling would not be required to be submitted and reviewed prior to approval of the PMA.)

11. An environmental assessment under 25.22(a)(18) (see page III-18 of the PMA Manual, "Environmental Impact Considerations"), unless the action qualifies for an exclusion (25.24(e)(4) or (5)). If the applicant believes that the action qualifies for exclusion, the PMA must provide information that establishes to FDA's satisfaction that the requested action is within the excluded category and meets the criteria for the applicable exclusion.

12. Such other information as FDA may request. If necessary, FDA will obtain the concurrence of the appropriate FDA advisory committee before requesting additional information.

Other information. Pertinent information already in FDA files and specifically referred to by an applicant may be incorporated into a PMA by reference. Information in a master file (see page III-1 of the PMA Manual for a detailed discussion of a master file) or other information submitted to FDA by a person other than the applicant will not be considered part of a PMA, unless such reference is authorized in writing by the person who submitted the information or the master file. If a master file is not referenced within five years after its submission to FDA, it will be returned to the person who submitted it.

Omissions. If an applicant believes that certain required information under 814.20(b) is not applicable to the device and omits any such information from its PMA, the applicant must submit a statement that identifies the omitted information and justifies the omission. The statement must be submitted as a separate section in the PMA and identified in the table of contents. If FDA does not accept the justification for the omission, the agency will notify the applicant. (Note: Required information (e.g., manufacturing information) may be temporarily omitted with acceptable justification. Refer to Item 31 in the preamble of the final order for additional information regarding the procedure to be followed and the conditions associated with it.)

Updates. An applicant must periodically update its pending application with any new safety and effectiveness information learned about the device from ongoing or completed studies that may affect an evaluation of the safety and effectiveness of the device or that may affect the statement of contraindications, warnings, precautions, and adverse reactions in the draft labeling. The update report must be consistent with the data-reporting provisions of the protocol. The applicant must submit three copies of any update report and must include in the report the PMA number assigned by FDA. These updates are considered to be amendments to the pending PMA. The time frame for review of a PMA will not be extended due to the submission of an update report unless the update is a major amendment (814.37(c)(1)). An applicant must submit these reports three months after the filing date, following receipt of an approvable letter, and at any other time as requested by FDA. (Note: This periodic updating is limited to studies sponsored by the applicant or to which the applicant has reasonable access.)

Color additive. If a color additive subject to Section 706 of the Act is used in or on the device and has not previously been listed for such use, an applicant (in lieu of submitting a color additive petition under Part 71) may submit the information as part of the PMA. When submitted as part of the PMA, the information must be submitted separately in three copies, each bound in one or more numbered volumes of reasonable size. A PMA for a device that contains a color additive that is subject to Section 706 of the Act will not be approved until the color additive is listed for use in or on the device.

Address. A PMA, an amendment, a supplement, or correspondence regarding a PMA must be sent to the PMA Document Mail Center (HFZ-401), Center for Devices and Radiological Health, Food and Drug Administration, 5600 Fishers Lane, Rockville, Maryland 20857.

PMA amendments and resubmitted PMAs (21 CFR 814.37)

An applicant may amend a pending PMA or PMA supplement to revise existing information or provide additional information. FDA may request that the applicant amend its PMA or PMA supplement with any necessary information about the device that FDA considers necessary to complete review of the PMA or PMA supplement.

A PMA amendment must include the PMA or PMA supplement number assigned to the original submission and, if submitted on the applicant's own initiative, the reason for submitting the amendment. For the following reasons, FDA may extend the time required for its review of the PMA or PMA supplement.

- If a major PMA amendment is submitted (e.g., an amendment that contains significant new data from a previously unreported study, significant updated data from a previously reported study, detailed new analyses of previously submitted data, or significant required information previously omitted) by the applicant on its own initiative or at FDA's request, the review period may be extended up to 180 days. If the amendment is not a major amendment, the review period will not be extended.
- If an applicant declines to submit a major amendment as requested by FDA, the review period may be extended for the number of days that elapse between the date of such request and the date that FDA receives the written response declining to submit the requested amendment.

An applicant may voluntarily withdraw its PMA or PMA supplement. If FDA requests an applicant to submit a PMA amendment and a written response to FDA's request is not received within 180 days, FDA will consider the pending PMA or PMA supplement to be withdrawn voluntarily by the applicant.

An applicant may resubmit a PMA or PMA supplement that was withdrawn, that FDA has refused to accept for filing, or that FDA has disapproved. A resubmitted PMA or PMA supplement must comply with the requirements of 814.20 or 814.39 and must include the PMA number assigned to the original submission as well as the applicant's reason for resubmission.

PMA supplements (21 CFR 814.39)

After FDA has approved a PMA, an applicant must submit a PMA supplement for review and approval by FDA before making any change affecting the safety or effectiveness of the device, unless the change is of a type for which FDA has advised that an alternate submission is permitted (see page I-13 of the PMA Manual for details). Changes for which an applicant must submit a PMA supplement include, but are not limited to, the following types of changes if they affect the safety or effectiveness of the device:

- new indication for use of the device;

- labeling changes;
- the use of a different facility or establishment to manufacture, process, or package the device;
- changes in manufacturing facilities, methods, or quality control procedures;
- changes in sterilization procedures;
- changes in packaging;
- changes in the performance or design specifications, circuits, components, ingredients, principles of operation, or physical layout of the device; and
- extension of the expiration date of the device based on data obtained under a new or revised stability or sterility testing protocol that has not been approved by FDA. If the protocol has been approved, the change must be reported to FDA in the postapproval periodic reports as described in the following paragraph (814.39(b)).

An applicant may make a change in a device after FDA's approval of the PMA without submitting a PMA supplement if (1) the change does not affect the device's safety or effectiveness, and (2) the change is reported to FDA in postapproval periodic reports required as a condition to approval of the device, e.g., an editorial change in labeling which does not affect the safety or effectiveness of the device. (Note: Trivial changes, such as changes in the color of a label, would not have to be included in the postapproval periodic report.)

All procedures and actions that apply to a PMA application under 814.20 also apply to PMA supplements, except that the information required in a supplement is limited to that needed to support the change. A summary is required only if there are new indications for use of the device, significant changes in the performance or design specifications, circuits, components, ingredients, principles of operation, or physical layout of the device, or when otherwise required by FDA. Three copies of a PMA supplement are required and must include information relevant to the proposed changes in the device. A PMA supplement must include a separate section that identifies each change for which approval is being requested and explains the reason for each change. The applicant must submit additional copies and information if requested by FDA. The time frames for review of a PMA supplement are the same as those provided for a PMA (814.40).

After FDA approves a PMA, any change described below that enhances the safety of the device or the safety in the use of the device (814.39(d)(2)) may be placed into effect by the applicant prior to the receipt of a written FDA order approving the PMA supplement provided that:

- the PMA supplement and its mailing cover are plainly marked "**Special PMA Supplement--Changes Being Effected;**"
- the PMA supplement provides a full explanation of the basis for the changes;
- the applicant has received acknowledgment from FDA of receipt of the supplement; and
- the PMA supplement specifically identifies the date that such changes are being effected.

The following changes are permitted [814.39(d)(1)]:

- o labeling changes that add or strengthen a contraindication, warning, precaution, or information about an adverse reaction;
- o labeling changes that add or strengthen an instruction that is intended to enhance the safe use of the device;
- o labeling changes that delete misleading, false, or unsupported indications; and
- o changes in quality controls or manufacturing process that add a new specification or test method, or otherwise provide additional assurance of purity, identity, strength, or reliability of the device.

30-day supplements and periodic reports

FDA will identify a change to a device for which the applicant has an approved PMA and for which a PMA supplement as described above is not required. Such changes will be identified in an advisory opinion (10.85) if the change applies to a generic type of device or in correspondence if the change applies only to the applicant's device.

FDA will require that a change, for which a PMA supplement as described above is not required, to be reported to FDA in a periodic report or a 30-day PMA supplement. In the advisory opinion or correspondence, FDA will identify the type of information that is to be included in the report or 30-day PMA supplement.

If the change must be reported to FDA in a periodic report, the change may be made before it is reported to FDA. If the change must be reported in a 30-day PMA supplement, the change may be made 30 days after FDA files the 30-day supplement, unless FDA informs the PMA holder that additional information is required, the supplement is not approvable, or the supplement is disapproved. The 30-day PMA supplement must follow the instructions in the correspondence or advisory opinion. Any 30-day PMA supplement that does not meet the requirements of the correspondence or advisory opinion will not be filed and, therefore, will not be deemed approved 30 days after receipt.

Subpart C - FDA Action on a PMA

Time frames for reviewing a PMA (21 CFR 814.40)

FDA must review a PMA within 180 days after receiving an application that is accepted for filing and to which the applicant does not submit a major amendment. FDA will review the PMA and, after receiving the recommendation of the appropriate FDA advisory committee, will send the applicant one of the following: an order approving the PMA [814.44(d)], an approvable letter [814.44(e)], a not-approvable letter [814.44(f)], or an order denying approval (814.45). The approvable letter and the not-approvable letter will provide an opportunity for the applicant to amend or withdraw the application, or to consider the letter to be a disapproval of the PMA (814.45). The applicant may request administrative review under Section 515(d)(3) and (g) of the Act.

Filing a PMA (21 CFR 814.42)

Within 45 days after FDA receives a PMA, the FDA will notify the applicant in writing whether the application has been filed. The filing of an application means that FDA has made a threshold determination that the application is sufficiently complete to permit a substantive review. The notice will include the PMA reference number and the date the FDA filed the PMA. (The date of filing is the date that a PMA accepted for filing was received by FDA.) The 180-day period for review of a PMA starts on the date of filing.

If FDA refuses to file a PMA, the FDA will notify the applicant of the reasons for the refusal. This notice will identify the deficiencies in the application that prevent filing and will include the PMA reference number.

If FDA refuses to file the PMA, the applicant has the following options:

- o The applicant may resubmit the PMA with additional information necessary to comply with the requirements of Section 515(c)(1)(A)-(G) of the Act and 814.20. A resubmitted PMA must include the PMA reference number of the original submission. If the resubmitted PMA is accepted for filing, the date of filing is the date FDA receives the resubmission.

- o The applicant may request, in writing, within 10 working days of the date of receipt of the FDA's notice refusing to file the PMA, an informal conference with the Director of the Office of Device Evaluation to review FDA's decision not to file the PMA. FDA will hold the informal conference within 10 working days after receiving the request and will make its decision on filing within 5 working days after the informal conference. If FDA then accepts the PMA for filing, the date of filing will be the date of the decision to accept the PMA for filing. If FDA does not reverse its decision, the applicant may request reconsideration of the decision from the Director of the Center for Devices and Radiological Health. The Director's decision will constitute final administrative action for the purpose of judicial review.

FDA may refuse to file a PMA if the FDA determines that any of the following apply:

- o the application is incomplete because it does not contain all the information required under Section 515(c)(1)(A)-(G) of the Act (see pages 8-3 and 8-4 of this chapter);

- o the PMA does not contain each of the items required under 814.20 and justification for omission of any item is inadequate;

- o the applicant has a pending premarket notification under Section 510(k) of the Act with respect to the same device, and FDA has not determined whether the device falls within the scope of 814.1(c); or

- o the PMA contains a false statement of material fact.

Procedures for review of a PMA (21 CFR 814.44)

FDA will begin substantive review of the PMA after it is accepted for filing (814.42). The PMA, or relevant portions, will be forwarded to each member of the appropriate FDA advisory committee for review. During the review process, FDA may communicate with the applicant [814.37(b)] or with the advisory committee to respond to questions that may be raised by committee members or to provide additional information. FDA will maintain a record of all communications with the applicant and with the advisory committee.

Before the advisory committee submits a final report to FDA, the committee must hold a public meeting to review the PMA in accordance with Part 14; this meeting may be held by telephone conference (14.22(g)). The advisory committee report and recommendation may be in the form of a meeting transcript signed by the chairperson of the committee. Within 180 days of the date of filing of the PMA, FDA will complete its review of the PMA and of the advisory committee's report and recommendation and issue one of the following: an order approving the PMA, an approvable letter, a not-approvable letter, or an order denying approval of the application.

After FDA reviews the committee's final report, the agency will notify the applicant that the PMA is approved if none of the reasons in 814.45 (see page I-17 of the PMA Manual) for denying approval of the application applies. FDA will approve an application on the basis of draft final labeling if the only deficiencies in the application concern editorial or similar minor deficiencies in the draft final labeling. Approval will be based on the condition that the applicant incorporates the specified labeling changes exactly as directed and submits to FDA a copy of the final printed labeling before marketing. FDA will notify the public of the approval and will include a notice of an opportunity for any interested person to request review (Section 515.(d)(3) of the Act). The notice of approval will be published in the FEDERAL REGISTER and will state that a detailed summary of information respecting the safety and effectiveness of the device has been placed on public display and that copies are available upon request. When a notice of approval is published, data and information in the PMA file will be available for public disclosure in accordance with 814.9.

FDA will send the applicant an approvable letter if the application substantially meets the requirements of the Act, and the FDA believes that it can approve the application if specific additional information is submitted or specific conditions are agreed to by the applicant.

The approvable letter will describe the information that FDA requires to be provided by the applicant or the conditions that the applicant is required to meet to obtain approval. FDA may require, for example, as a condition to approval:

- o the submission of certain information identified in the approvable letter, such as final labeling;
- o an FDA inspection that finds the manufacturing facilities, methods, and controls in compliance with the good manufacturing practices regulations (Part 820) and, if applicable, verification of records pertinent to the PMA;
- o restrictions imposed on the sale, distribution, or use of the device under Section 515(d)(1)(B)(ii) or 520(e) of the Act; or
- o postapproval requirements (see page I-19 of the PMA Manual).

In response to an approvable letter, the applicant may:

- o amend the PMA as requested;
- o consider the approvable letter to be a denial of the PMA (814.45) and request administrative review (Section 515(d)(3) of the Act) by filing a petition for reconsideration (10.33); or
- o withdraw the PMA.

FDA will send the applicant a not-approvable letter if the FDA believes that the application may not be approved for one or more of the reasons given in 814.45(a). The not-approvable letter will describe the deficiencies in the application, including each applicable ground for denial under Section 515(d)(2)(A)-(E) of the Act. Where practical, FDA will identify what is necessary to make the PMA approvable. In response to a not-approvable letter, the applicant may:

- amend the PMA as requested [such an amendment will be considered a major amendment under 814.37(c)(1)];
- consider the not-approvable letter to be a denial of approval of the PMA (814.45) and request administrative review (Section 515(d)(3) of the Act) by filing a petition for reconsideration (10.33); or
- withdraw the PMA.

FDA will consider a PMA to have been withdrawn voluntarily if:

- the applicant fails to respond in writing to a written request for an amendment within 180 days after the date FDA issues such request;
- the applicant fails to respond in writing to an approvable or not-approvable letter within 180 days after the date FDA issues such letter; or
- the applicant submits a written notice to FDA that the PMA has been withdrawn.

Denial of approval of a PMA (21 CFR 814.45)

FDA may deny approval of a PMA if the applicant fails to follow the requirements of this regulation or if (upon the basis of the information in the PMA or any other information before the FDA) FDA determines that any of the grounds for denying approval of a PMA specified in Section 515(d)(2)(A)-(E) of the Act applies. In addition, FDA may deny approval of a PMA for any of the following reasons.

- The PMA contains a false statement of material fact.
- The device's proposed labeling does not comply with the requirements in Part 801 (Labeling) or Part 809 (In Vitro Diagnostic Products for Human Use).
- The applicant does not permit an authorized FDA employee to inspect the facilities and controls in which the device will be manufactured, to have access to all records pertinent to the application, and to copy and verify any pertinent records.
- An essential nonclinical laboratory study described in the PMA was not conducted in compliance with the Good Laboratory Practice regulations in Part 58 and no reason for the noncompliance is provided, or, if it is, the differences between the practice used in conducting the study and the Good Laboratory Practice regulations do not support the validity of the study.
- Any clinical investigation involving human subjects described in the PMA, subject to the Institutional Review Board regulations in Part 56 or Informed Consent regulations in Part 50, was not conducted in compliance with these regulations such that the rights or safety of human subjects were not adequately protected.

FDA will issue any order denying approval of a PMA in accordance with 814.17. The order will inform the applicant of the deficiencies in the PMA, including each applicable ground for denial under Section 515(d)(2) of the Act and the regulations under Part 814, and, where practical, will identify measures required to place the PMA in approvable form. The order will include a notice of an opportunity to request review under Section 515(d)(3) of the Act.

FDA will use the criteria specified in 860.7 (Determination of Safety and Effectiveness) in deciding whether to approve or deny approval of a PMA. FDA may use information other than that submitted by the applicant in making such determination.

FDA will publish a FEDERAL REGISTER notice of an order denying approval of the PMA. The notice will state that a detailed summary of information concerning the safety and effectiveness of the device has been placed on public display and that copies are available upon request. When a notice of denial of approval is made publicly available, data and information in the PMA file will be available for public disclosure (814.9). FDA will issue an order denying approval of a PMA after an approvable or not-approvable letter has been sent and the applicant has:

- o submitted the requested amendment but any ground for denying approval under Section 515(d)(2) of the Act still applies; or
- o notified FDA in writing that the requested amendment will not be submitted; or
- o petitioned for review under Section 515(d)(3) of the Act by filing a petition in the form of a petition for reconsideration (10.33).

Withdrawal of approval of a PMA (21 CFR 814.46)

FDA may issue an order withdrawing approval of a PMA if the FDA determines from any information available that:

- o any of the grounds under Section 515(e)(1)(A)-(G) of the Act apply;
- o any postapproval requirement imposed by the PMA approval order or by regulation has not been met;
- o an essential laboratory study described in the PMA was not conducted in compliance with the Good Laboratory Practice regulations in Part 58 and no reason for the noncompliance is provided or, if it is, the differences between the practices used in conducting the study and the Good Laboratory Practice regulation do not support the validity of the study; or
- o any clinical investigation involving human subjects described in the PMA, subject to the Institutional Review Board regulations in Part 56 or Informed Consent regulations in Part 50, was not conducted in compliance with these regulations, such that the rights or safety of human subjects were not adequately protected.

FDA may seek advice on scientific matters from any appropriate FDA advisory committee in deciding whether to withdraw approval of a PMA. FDA may also use information other than that submitted by the applicant in deciding whether to withdraw approval of a PMA.

Before issuing an order to withdraw approval of a PMA. FDA will issue the holder of the approved application a notice of opportunity for an informal hearing under Part 16. If the applicant does not request a hearing or if after the Part 16 hearing is held the agency decides to proceed with the withdrawal. FDA will issue an order withdrawing approval of the application. The order (814.17) will state each ground for withdrawing approval and will include a notice of an opportunity for administrative review under Section 515(e)(2) of the Act.

FDA will publish a FEDERAL REGISTER notice of an order withdrawing approval of a PMA. The notice will state that a detailed summary of information concerning the safety and effectiveness of the device has been placed on public display and that copies are available upon request. When a notice of withdrawal of approval is published. data and information in the PMA file will be available for public disclosure (814.9).

Subpart D - Administrative Review (Reserved)

Subpart E - Postapproval Requirements

General (21 CFR 814.80)

A device may not be manufactured. packaged. stored. labeled. distributed. or advertised in a manner that is inconsistent with any conditions to approval specified in the PMA approval order for the device.

Postapproval requirements (21 CFR 814.82)

FDA may impose postapproval requirements in a PMA approval order or by regulation at the time of approval of the PMA or by regulation subsequent to approval. Postapproval requirements may include as a condition of approval of the device:

o restriction of the sale. distribution or use of the device (Section 515(d)(1)(B)(ii) or 520(e) of the Act):

o continuing evaluation and periodic reporting on the safety. effectiveness. and reliability of the device for its intended use:

(Note: FDA will state in the PMA approval order the reason or purpose for such a requirement and the number of patients to be evaluated and the reports required to be submitted.)

o prominent display in the labeling of a device and in the advertising of any restricted device of warnings. hazards or precautions important for the device's safe and effective use. including patient information (e.g.. information provided to the patient on alternative modes of therapy and on risks and benefits associated with the use of the device):

o inclusion of identification codes on the device or its labeling or. in the case of an implant. on cards given to patients if necessary to protect the public health:

(Note: If patient identification cards are required in cases where the devices are sold directly to health practitioners. a PMA applicant's responsibility will be to supply such cards directly to practitioners for distribution to patients and to take reasonable steps to obtain patient identity information from the practitioners.)

- maintenance of records that will enable the applicant to submit to FDA information needed to trace patients if such information is necessary to protect the public health;

  (Note: Under Section 519(a)(4) of the Act, FDA will require that the identity of any patient be disclosed in records maintained under the postapproval reporting requirements only to the extent required for the medical welfare of the individual, to determine the safety or effectiveness of the device, or to verify a record, report or information submitted to the agency.)

- maintenance of records for specified periods of time and organization and indexing of records into identifiable files to enable FDA to determine whether there is reasonable assurance of the continued safety and effectiveness of the device;
- at specified intervals, submission of periodic reports containing the information required by 814.84(b);
- batch testing of the device; and
- any other requirements determined by FDA to be necessary to provide reasonable assurance, or continued reasonable assurance, of the safety and effectiveness of the device.

An applicant must grant FDA access to any records and reports required under the provision of 814.82 and permit authorized FDA employees to copy and verify such records and reports and to inspect at a reasonable time and in a reasonable manner all manufacturing facilities to verify that the device is being manufactured, stored, labeled, and shipped under approved conditions.

Failure to comply with any postapproval requirement constitutes a ground for withdrawing approval of a PMA.

Reports (21 CFR 814.84)

The holder of an approved PMA must comply with the requirements of Part 803 (Medical Device Reporting) and with any other requirements applicable to the device by other regulations or by order approving the device.

Unless FDA specifies otherwise, any periodic report must:

- identify changes described in 814.39(a) and changes required to be reported to FDA under 814.39(b); and
- contain a bibliography and summary of the following information that was not previously submitted as part of the PMA and that is known to or reasonably should be known to the applicant: (1) unpublished reports of data from any clinical investigations or nonclinical laboratory studies involving the device or related devices, and (2) reports in the scientific literature concerning the device.

  (Note: "Related" devices shall mean devices that are the same or substantially similar.)

If, after reviewing the bibliography and summary, FDA concludes that the agency needs a copy of the unpublished or published reports, FDA will notify the applicant that copies of such reports must be submitted.

PRODUCT DEVELOPMENT PROTOCOLS

Section 515(f) of the Act authorizes the use of the Product Development Protocol (PDP) procedure for gaining marketing approval for a Class III medical device. The investigation of a device and the development of necessary information for marketing approval are merged into one regulatory mechanism.

To find out if the PDP approach is available or appropriate, manufacturers may consult with the FDA. Appropriateness of a PDP over the IDE/PMA or reclassification petition approaches would depend on whether:

(1) the device is innovative;

(2) the device offers significant health benefits and FDA believes that use of the PDP will result in realizing those benefits more quickly than the IDE/PMA process;

(3) FDA believes that the sponsor's device will work and that proposals for testing the device will demonstrate the device's safety and effectiveness;

(4) there is adequate information about the device to permit a decision;

(5) the device offers significant public health benefit, but has limited market potential or significant development costs, warranting FDA cooperation through the PDP process to minimize such costs; and

(6) there is reason to believe that the risks to the subjects are outweighed by the anticipated benefits to the subjects and the importance of the knowledge to be gained.

Generally, FDA would not consider a PDP appropriate in situations where:

(1) preclinical testing appears to be too far advanced for the PDP to be advantageous;

(2) the sponsor has a pending petition for reclassification of the device, or another sponsor has a pending petition for reclassification of a device of the same generic class;

(3) the sponsor has a current IDE, PMA, or premarket notification 510(k) under review by FDA for the same device; or

(4) the device is a preamendments Class III device (unless unusual circumstances are shown).

A guideline prescribing the content of a PDP is available upon request from the Division of Small Manufacturers Assistance.

FDA 86-4208	Medical Device Federal Register Documents (Revised June 1986) (PB 87-115481/AS, $13.95).
FDA 86-4209	An Introduction to Transcutaneous Electrical Nerve Stimulation: TENS (PB 87-107884/AS, $11.95).
FDA 86-4210	A Comprehensive Review of Hemodialysis Equipment and Related Peripheral Support Equipment: Efficacy, Efficiency and Safety (Volumes I and II) (PB 86-245404/AS, $28.95).
FDA 86-4211	Hemodialysis Equipment and Practices in Massachusetts (PB 86-242427/AS, $11.95).
FDA 86-4212	Protocol for the Study of Hemodialysis in Ohio (PB 86-245370/AS, $22.95).
FDA 86-4213	State Participation in Dialysis System Investigation (PB 87-108825/AS, $24.95).
FDA 87-4002	Impact Resistant Lenses. Questions and Answers - June 1972 (FDA 81-4002) (Revised September 1987) (PB 88-123021/AS, $12.95).
FDA 87-4179	Device Good Manufacturing Practices Manual - November 1985 (Revised November 1987) (GPO 017-012-00330-3, $18.00) (PB 88-132139, $38.95).
FDA 87-4188	Need Help With Medical Device Regulations? Contact DSMA (supersedes FDA 84-4188) (pamphlet).
FDA 87-4199	Medical Device Establishment Registration - Information and Instructions May 1987 (supersedes FDA 85-4199) (PB 88-123666/AS, $12.95).
FDA 87-4214	Premarket Approval (PMA) Manual (October 1986) (GPO 017-012-00329-0, $7.50) (PB 87-154365/AS, $18.95).
FDA 87-4215	Orthopaedic Device Labeling -- Guideposts for Concerned Physicians (January 1987) (flyer).
FDA 87-4217	Proceedings of the First International Conference of Medical Devices Regulatory Authorities (ICMDRA) - June 2-6, 1986 (PB 88-123005/AS, $25.95).
FDA 87-4218	Have a New Medical Device? (brochure).
FDA 87-4219	Medical Devices Standards Activities Report (PB 88-123641/AS, $19.95).
FDA 87-4221	Regulatory Requirements for Devices for the Handicapped (PB 88-123013/AS, $12.95).
FDA 87-4222	An Introduction to Medical Device Regulations (pamphlet).
FDA 87-4223	Classifying Your Medical Devices (brochure).
FDA 87-4224	In Vitro Diagnostic Devices: Guidance for the Preparation of 510(k) Submissions (GPO 017-012-00331-1, $3.50) (PB 88-121801/AS, $14.95).
FDA 88-4160	Import and Export - Regulatory Requirements for Medical Devices (August 1988)(GPO 017-012-00336-2, $2.25) (PB 89-121859/AS, $13.95).
FDA 88-4225	Review and Summary of Hemodialysis System Investigative Reports from California, the District of Columbia, Massachusetts and Ohio (PB 88-121793/AS, $19.95).
FDA 88-4226	Medical Device Reporting Questions and Answers (February 1988) (PB 88-192737/AS, $14.95).
FDA 88-4227	Export of Medical Devices: A Workshop Manual (September 1988) (GPO 017-012-00338-9, $10.00) (PB 89-119663/AS, $28.95).
FDA 88-4228	Import of Medical Devices: A Workshop Manual (September 1988) (GPO 017-012-00337-1, $8.50) (PB 89-119671/AS, $21.95).
FDA 88-4229	Applications of DNA Probes for the Diagnosis of Human Infectious Diseases: An Overview (September 1988) (GPO 017-012-00340-1, $2.00) (PB 89-120497/AS, $15.95).
FDA 89-4158	Premarket Notification: 510(k) - Regulatory Requirements for Medical Devices (November 1988) (GPO 017-012-00342-7, $3.75).

U.S. DEPARTMENT OF
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